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(57) Abstract

The present invention relates generally to isolated genes which encode polypeptides involved in cellulose biosynthesis in plants and transgenic plants expressing same in sense or antisense orientation, or as ribozymes, co-suppression or gene-targeting molecules. More particularly, the present invention is directed to a nucleic acid molecule isolated from Arabidopsis thaliana, Oryza sativa, wheat, barley, maize, Brassica ssp., Gossypium hirsutum and Eucahyptus ssp. which encode an enzyme which is important in cellulose biosynthesis, in particular the cellulose synthase enzyme and homologues, analogues and derivatives thereof and uses of same in the production of transgenic plants expressing altered cellulose biosynthetic properties.

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"MANIPULATION OF CELLULOSE AND/OR β-1,4-GLUCAN"

The present invention relates generally to isolated genes which encode polypeptides involved in cellulose biosynthesis and transgenic organisms expressing same in sense or antisense or orientation, or as ribozymes, co-suppression or gene-targeting molecules. More particularly, the present invention is directed to a nucleic acid molecule isolated from Arabidopsis thaliana, Oryza sativa, wheat, barley, maize, Brassica ssp., Gossypium hirsutum and Eucalyptus ssp. which encode an enzyme which is important in cellulose biosynthesis, in particular the cellulose synthase enzyme and homologues, analogues and derivatives thereof and uses of same in the production of transgenic plants expressing altered cellulose biosynthetic properties.

Bibliographic details of the publications referred to by author in this specification are collected at the end of the description. Sequence identity numbers (SEQ ID Nos.) for the nucleotide and amino acid sequences referred to in the specification are defined after the bibliography.

Throughout the specification, unless the context requires otherwise, the word "comprise", or variations such as "comprises" or "comprising" will be understood to imply the inclusion of 20 a stated element or integer or group of elements or integers but not the exclusion of any other element or integer or group of elements or integers.

Cellulose, the world's most abundant biopolymer, is the most characteristic component of plant cell walls in so far as it forms much of the structural framework of the cell wall.

25 Cellulose is comprised of crystalline β-1,4-glucan microfibrils. The crystalline microfibrils are extremely strong and resist enzymic and mechanical degradation, an important factor in determining the nutritional quantity, digestibility and palatability of animal and human foodstuffs. As cellulose is also the dominant structural component of industrially-important plant fibres, such as cotton, flax, hemp, jute and the timber crops such as Eucalyptus ssp. and

30 Pinus ssp., amongst others, there is considerable economic benefit to be derived from the

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manipulation of cellulose content and/or quantity in plants. In particular, the production of food and fibre crops with altered cellulose content are highly desirable objectives.

The synthesis of cellulose involves the β -1,4-linkage of glucose monomers, in the form of a nucleoside diphospoglucose such as UDP-glucose, to a pre-existing cellulose chain, catalysed by the enzyme cellulose synthase.

Several attempts to identify the components of the functional cellulose synthase in plants have failed, because levels of β -1,4-glucan or crystalline cellulose produced in such assays have 10 hitherto been too low to permit enzyme purification for protein sequence determination. Insufficient homology between bacterial β -1,4-glucan synthase genes and plant cellulose synthase genes has also prevented the use of hybridisation as an approach to isolating the plant homologues of bacterial β -1,4-glucan (cellulose) synthases.

15 Furthermore, it has not been possible to demonstrate that the cellulose synthase enzyme from plants is the same as, or functionally related to, other purified and characterised enzymes involved in polysaccharide biosynthesis. As a consequence, the cellulose synthase enzyme has not been isolated from plants and, until the present invention, no nucleic acid molecule has been characterised which functionally-encodes a plant cellulose synthase enzyme.

20

In work leading up to the present invention, the inventors have generated several novel mutant Arabidopsis thaliana plants which are defective in cellulose biosynthesis. The inventors have further isolated a cellulose synthase gene designated RSW1, which is involved in cellulose biosynthesis in Arabidopsis thaliana, and homologous sequences in Oryza sativa, wheat, barley, maize, Brassica ssp., Gossypium hirsutum and Eucalyptus ssp. The isolated nucleic acid molecules of the present invention provide the means by which cellulose content and structure may be modified in plants to produce a range of useful fibres suitable for specific industrial purposes, for example increased decay resistance of timber and altered digestibility of foodstuffs, amongst others.

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Accordingly, one aspect of the present invention provides an isolated nucleic acid molecule comprising a sequence of nucleotides which encodes, or is complementary to a sequence which encodes a polypeptide of the cellulose biosynthetic pathway or a functional homologue, analogue or derivative thereof.

5

The nucleic acid molecule of the invention may be derived from a prokaryotic source or a eukaryotic source.

Those skilled in the art will be aware that cellulose production requires not only the presence of a catalytic subunit, but also its activation and organisation into arrays which favour the crystallization of glucan chains. This organisation is radically different between bacteria, which possess linear arrays, and higher plants, which possess hexameric clusters or "rosettes", of glucan chains. The correct organisation and activation of the bacterial enzyme may require many factors which are either not known, or alternatively, not known to be present in plant cells, for example specific membrane lipids to impart an active conformation on the enzyme complex or protein, or the bacterial c-di-GMP activation system. Accordingly, the use of a plant-derived sequence in eukaryotic cells such as plants provides significant advantages compared to the use of bacterially-derived sequences.

- 20 Accordingly, the present invention does not extend to known genes encoding the catalytic subunit of Agrobacterium tumefaciens or Acetobacter xylinum or Acetobacter pasteurianus cellulose synthase, or the use of such known bacterial genes and polypeptides to manipulate cellulose.
- 25 Preferably, the subject nucleic acid molecule is derived from an eukaryotic organism.

In a more preferred embodiment of the invention, the isolated nucleic acid molecule of the invention encodes a plant cellulose synthase or a catalytic subunit thereof, or a homologue, analogue or derivative thereof.

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More preferably, the isolated nucleic acid molecule encodes a plant cellulose synthase polypeptide which is associated with the primary cell wall of a plant cell. In an alternative preferred embodiment, the nucleic acid molecule of the invention encodes a plant cellulose synthase or catalytic subunit thereof which is normally associated with the secondary cell wall 5 of a plant cell.

In a more preferred embodiment, the nucleic acid molecule of the invention is a cDNA molecule, genomic clone, mRNA molecule or a synthetic oligonucleotide molecule.

In a particularly preferred embodiment, the present invention provides an isolated nucleic acid molecule which encodes or is complementary to a nucleic acid molecule which encodes the *Arabidopsis thaliana*, *Gossypium hirsutum* (cotton), *Oryza sativa* (rice), *Eucalyptus ssp.*, *Brassica ssp.* wheat, barley or maize cellulose synthase enzyme or a catalytic subunit thereof or a polypeptide component, homologue, analogue or derivative thereof.

15

As exemplified herein, the present inventors have identified cellulose biosynthesis genes in maize, wheat, barley, rice, cotton, *Brassica ssp.* and *Eucalyptus ssp.*, in addition to the specific *Arabidopsis thaliana RSW*1 gene sequence which has been shown to be particularly useful for altering cellulose and/or β -1,4-glucan and/or starch levels in cells.

20

Hereinafter the term "polypeptide of the cellulose biosynthetic pathway" or similar term shall be taken to refer to a polypeptide or a protein or a part, homologue, analogue or derivative thereof which is involved in one or more of the biosynthetic steps leading to the production of cellulose or any related β-1,4-glucan polymer in plants. In the present context, a polypeptide of the cellulose biosynthetic pathway shall also be taken to include both an active enzyme which contributes to the biosynthesis of cellulose or any related β-1,4-glucan polymer in plants and to a polypeptide component of such an enzyme. As used herein, a polypeptide of the cellulose biosynthetic pathway thus includes cellulose synthase. Those skilled in the art will be aware of other cellulose biosynthetic pathway polypeptides in plants.

The term "related β-1,4-glucan polymer" shall be taken to include any carbohydrate molecule comprised of a primary structure of β-1,4-linked glucose monomers similar to the structure of the components of the cellulose microfibril, wherein the relative arrangement or relative configuration of the glucan chains may differ from their relative configuration in microfibrils of cellulose. As used herein, a related β-1,4-glucan polymer includes those β-1,4-glucan polymers wherein individual β-1,4-glucan microfibrils are arranged in an anti-parallel or some other relative configuration not found in a cellulose molecule of plants and those non-crystalline β-1,4-glucans described as lacking the resistance to extraction and degradation that characterise cellulose microfibrils.

10

The term "cellulose synthase" shall be taken to refer to a polypeptide which is required to catalyse a β -1,4-glucan linkage to a cellulose microfibril.

Reference herein to "gene" is to be taken in its broadest context and includes:

- 15 (i) a classical genomic gene consisting of transcriptional and/or translational regulatory sequences and/or a coding region and/or non-translated sequences (i.e. introns, 5'- and 3'- untranslated sequences); or
 - (ii) mRNA or cDNA corresponding to the coding regions (i.e. exons) and 5'- and 3'- untranslated sequences of the gene.

20

The term "gene" is also used to describe synthetic or fusion molecules encoding all or part of a functional product.

In the present context, the term "cellulose gene" or "cellulose genetic sequence" or similar term shall be taken to refer to any gene as hereinbefore defined which encodes a polypeptide of the cellulose biosynthetic pathway and includes a cellulose synthase gene.

The term "cellulose synthase gene" shall be taken to refer to any cellulose gene which specifically encodes a polypeptide which is a component of a functional enzyme having 30 cellulose synthase activity i.e. an enzyme which catalyses a β-1,4-glucan linkage to a

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cellulose microfibril.

Preferred cellulose genes may be derived from a naturally-occurring cellulose gene by standard recombinant techniques. Generally, a cellulose gene may be subjected to 5 mutagenesis to produce single or multiple nucleotide substitutions, deletions and/or additions. Nucleotide insertional derivatives of the cellulose synthase gene of the present invention include 5' and 3' terminal fusions as well as intra-sequence insertions of single or multiple nucleotides. Insertional nucleotide sequence variants are those in which one or more nucleotides are introduced into a predetermined site in the nucleotide sequence although random insertion is also possible with suitable screening of the resulting product. Deletional variants are characterised by the removal of one or more nucleotides from the sequence. Substitutional nucleotide variants are those in which at least one nucleotide in the sequence has been removed and a different nucleotide inserted in its place. Such a substitution may be "silent" in that the substitution does not change the amino acid defined by the codon.

15 Alternatively, substituents are designed to alter one amino acid for another similar acting amino acid, or amino acid of like charge, polarity, or hydrophobicity.

As used herein, the term "derived from" shall be taken to indicate that a particular integer or group of integers has originated from the species specified, but has not necessarily been 20 obtained directly from the specified source.

For the present purpose, "homologues" of a nucleotide sequence shall be taken to refer to an isolated nucleic acid molecule which is substantially the same as the nucleic acid molecule of the present invention or its complementary nucleotide sequence, notwithstanding the occurrence within said sequence, of one or more nucleotide substitutions, insertions, deletions, or rearrangements.

"Analogues" of a nucleotide sequence set forth herein shall be taken to refer to an isolated nucleic acid molecule which is substantially the same as a nucleic acid molecule of the present invention or its complementary nucleotide sequence, notwithstanding the occurrence of any

non-nucleotide constituents not normally present in said isolated nucleic acid molecule, for example carbohydrates, radiochemicals including radionucleotides, reporter molecules such as, but not limited to DIG, alkaline phosphatase or horseradish peroxidase, amongst others.

5 "Derivatives" of a nucleotide sequence set forth herein shall be taken to refer to any isolated nucleic acid molecule which contains significant sequence similarity to said sequence or a part thereof. Generally, the nucleotide sequence of the present invention may be subjected to mutagenesis to produce single or multiple nucleotide substitutions, deletions and/or insertions. Nucleotide insertional derivatives of the nucleotide sequence of the present invention include 10 5° and 3° terminal fusions as well as intra-sequence insertions of single or multiple nucleotides or nucleotide analogues. Insertional nucleotide sequence variants are those in which one or more nucleotides or nucleotide analogues are introduced into a predetermined site in the nucleotide sequence of said sequence, although random insertion is also possible with suitable screening of the resulting product being performed. Deletional variants are characterised by the removal of one or more nucleotides from the nucleotide sequence. Substitutional nucleotide variants are those in which at least one nucleotide in the sequence has been removed and a different nucleotide or nucleotide analogue inserted in its place.

The present invention extends to the isolated nucleic acid molecule when integrated into the genome of a cell as an addition to the endogenous cellular complement of cellulose synthase genes. The said integrated nucleic acid molecule may, or may not, contain promoter sequences to regulate expression of the subject genetic sequence.

The isolated nucleic acid molecule of the present invention may be introduced into and expressed in any cell, for example a plant cell, fungal cell, insect cell, animal cell, yeast cell or bacterial cell. Those skilled in the art will be aware of any moficiations which are required to the codon usage or promoter sequences or other regulatory sequences, in order for expression to occur in such cells.

30 Another aspect of the present invention is directed to a nucleic acid molecule which comprises

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a sequence of nucleotides corresponding or complementary to any one or more of the sequences set forth in SEQ ID Nos:1, 3, 4, 5, 7, 9, 11, or 13, or having at least about 40%, more preferably at least about 55%, still more preferably at least about 65%, yet still more preferably at least about 75-80% and even still more preferably at least about 85-95% nucleotide similarity to all, or a part thereof.

According to this aspect of the invention, said nucleic acid molecule encodes, or is complementary to a nucleotide sequence encoding, a polypeptide of the cellulose biosynthetic pathway in a plant or a homologue, analogue or derivative thereof.

10

Preferably, a nucleic acid molecule which is at least 40% related to any one or more of the sequences set forth in SEQ ID Nos:1, 3, 4, 5, 7, 9, 11, or 13 comprises a nucleotide sequence which encodes or is complementary to a sequence which encodes a plant cellulose synthase, more preferably a cellulose synthase which is associated with the primary or the 15 secondary plant cell wall of the species from which it has been derived.

Furthermore, the nucleic acid molecule according to this aspect of the invention may be derived from a monocotyledonous or dicotyledonous plant species. In a particularly preferred embodiment, the nucleic acid molecule is derived from *Arabidopsis thaliana*, *Oryza sativa*, 20 wheat, barley, maize, *Brassica ssp.*, *Gossypium hirsutum* (cotton) or *Eucalyptus ssp.*, amongst others.

For the purposes of nomenclature, the nucleotide sequence shown in SEQ ID NO:1 relates to a cellulose gene as hereinbefore defined which comprises a cDNA sequence designated T20782 and which is derived from *Arabidopsis thaliana*. The amino acid sequence set forth in SEQ ID NO:2 relates to the polypeptide encoded by T20782.

The nucleotide sequence set forth in SEQ ID NO:3 relates to the nucleotide sequence of the complete *Arabidopsis thaliana* genomic gene *RSW*1, including both intron and exon sequences. The nucleotide sequence of SEQ ID NO:3 comprises exons 1-14 of the genomic

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gene and includes 2295bp of 5'-untranslated sequences, of which approximately the first 1.9kb comprises RSW1 promoter sequence (there is a putative TATA box motif at positions 1843-1850 of SEQ ID NO:3). The nucleotide sequence set forth in SEQ ID NO:3 is derived from the cosmid clone 23H12. This sequence is also the genomic gene equivalent of SEQ ID No:1 and 5.

The nucleotide sequence set forth in SEQ ID NO:4 relates to the partial nucleotide sequence of a genomic gene variant of RSW1, derived from cosmid clone 12C4. The nucleotide sequence of SEQ ID NO:4 comprises exon sequence 1-11 and part of exon 12 of the genomic gene sequence and includes 862bp of 5'-untranslated sequences, of which approximately 700 nucleotides comprise RSW1 promoter sequences (there is a putative TATA box motif at positions 668-673 of SEQ ID NO:4). The genomic gene sequence set forth in SEQ ID NO:4 is the equivalent of the cDNA sequence set forth in SEQ ID NO:7 (i.e. cDNA clone Ath-A).

15 The nucleotide sequence shown in SEQ ID NO:5 relates to a cellulose gene as hereinbefore defined which comprises a cDNA equivalent of the *Arabidopsis thaliana RSW*1 gene set forth in SEQ ID NO:3. The amino acid sequence set forth in SEQ ID NO:6 relates to the polypeptide encoded by the wild-type *RSW*1 gene sequences set forth in SEQ ID Nos:3 and 5.

20

The nucleotide sequence shown in SEQ ID NO:7 relates to a cellulose gene as hereinbefore defined which comprises a cDNA equivalent of the *Arabidopsis thaliana RSW*1 gene set forth in SEQ ID NO:4. The nucleotide sequence is a variant of the nucleotide sequences set forth in SEQ ID Nos:3 and 5. The amino acid sequence set forth in SEQ ID NO:8 relates to the polypeptide encoded by the wild-type *RSW*1 gene sequences set forth in SEQ ID Nos:4 and 6.

The nucleotide sequence shown in SEQ ID NO:9 relates to a cellulose gene as hereinbefore defined which comprises a further wild-type variant of the *Arabidopsis thaliana RSW*1 gene 30 set forth in SEQ ID Nos:3 and 5. The nucleotide sequence variant is designated *Ath-B*. The

amino acid sequence set forth in SEQ ID NO:10 relates to the polypeptide encoded by the wild-type RSW1 gene sequence set forth in SEQ ID No:9.

The nucleotide sequence shown in SEQ ID NO:11 relates to a cellulose gene as hereinbefore defined which comprises a cDNA equivalent of the *Arabidopsis thaliana rsw*1 gene. The *rsw*1 gene is a mutant cellulose gene which produces a radial root swelling phenotype as described by Baskin *et al* (1992). The present inventors have shown herein that the *rsw*1 gene also produces reduced inflorescence length, reduced fertility, misshapen epidermal cells, reduced cellulose content and the accumulation of non-crystalline β-1,4-glucan, amongst others, when expressed in plant cells. The *rsw*1 nucleotide sequence is a further variant of the nucleotide sequences set forth in SEQ ID Nos:3 and 5. The amino acid sequence set forth in SEQ ID NO:12 relates to the rsw1 polypeptide encoded by the mutant *rsw*1 gene sequence set forth in SEQ ID No:11.

15 The nucleotide sequence shown in SEQ ID NO:13 relates to a cellulose gene as hereinbefore defined which comprises a cDNA equivalent of the *Oryza sativa RSW*1 or *RSW*1-like gene. The nucleotide sequence is closely-related to the *Arabidopsis thaliana RSW*1 and *rsw*1 nucleotide sequences set forth herein (SEQ ID Nos:1, 3, 4, 5, 7, 9 and 11). The amino acid sequence set forth in SEQ ID NO:14 relates to the polypeptide encoded by the *RSW*1 or 20 *RSW*1-like gene sequences set forth in SEQ ID No:13.

Those skilled in the art will be aware of procedures for the isolation of further cellulose genes to those specifically described herein, for example further cDNA sequences and genomic gene equivalents, when provided with one or more of the nucleotide sequences set forth in SEQ 25 ID Nos:1, 3, 4, 5, 7, 9, 11, or 13. In particular, hybridisations may be performed using one or more nucleic acid hybridisation probes comprising at least 10 contiguous nucleotides and preferably at least 50 contiguous nucleotides derived from the nucleotide sequences set forth herein, to isolate cDNA clones, mRNA molecules, genomic clones from a genomic library (in particular genomic clones containing the entire 5' upstream region of the gene including 30 the promoter sequence, and the entire coding region and 3'-untranslated sequences), and/or

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synthetic oligonucleotide molecules, amongst others. The present invention clearly extends to such related sequences.

The invention further extends to any homologues, analogues or derivatives of any one or 5 more of SEQ ID Nos:1, 3, 4, 5, 7, 9, 11 or 13.

A further aspect of the present invention contemplates a nucleic acid molecule which encodes or is complementary to a nucleic acid molecule which encodes, a polypeptide which is required for cellulose biosynthesis in a plant, such as cellulose synthase, and which is capable of hybridising under at least low stringency conditions to the nucleic acid molecule set forth in any one or more of SEQ ID Nos:1, 3, 4, 5, 7, 9, 11 or 13, or to a complementary strand thereof.

As an exemplification of this embodiment, the present inventors have shown that it is possible to isolate variants of the *Arabidopsis thaliana RSW*1 gene sequence set forth in SEQ ID NO:3, by hybridization under low stringency conditions. Such variants include related sequences derived from *Gossypium hirsutum* (cotton), *Eucalyptus ssp.* and *A. thaliana*. Additional variant are clearly encompassed by the present invention.

20 Preferably, the nucleic acid molecule further comprises a nucleotide sequence which encodes, or is complementary to a nucleotide sequence which encodes, a cellulose synthase polypeptide, more preferably a cellulose synthase which is associated with the primary or secondary plant cell wall of the plant species from which said nucleic acid molecule was derived.

25

More preferably, the nucleic acid molecule according to this aspect of the invention encodes or is complementary to a nucleic acid molecule which encodes, a polypeptide which is required for cellulose biosynthesis in a plant, such as cellulose synthase, and which is capable of hybridising under at least medium stringency conditions to the nucleic acid molecule set 30 forth in any one or more of SEQ ID Nos:1, 3, 4, 5, 7, 9, 11 or 13, or to a complementary

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strand thereof.

Even more preferably, the nucleic acid molecule according to this aspect of the invention encodes or is complementary to a nucleic acid molecule which encodes, a polypeptide which 5 is required for cellulose biosynthesis in a plant, such as cellulose synthase, and which is capable of hybridising under at least high stringency conditions to the nucleic acid molecule set forth in any one or more of SEQ ID Nos:1, 3, 4, 5, 7, 9, 11 or 13, or to a complementary strand thereof.

10 For the purposes of defining the level of stringency, a low stringency is defined herein as being a hybridisation and/or a wash carried out in 6xSSC buffer, 0.1% (w/v) SDS at 28°C. Generally, the stringency is increased by reducing the concentration of SSC buffer, and/or increasing the concentration of SDS and/or increasing the temperature of the hybridisation and/or wash. A medium stringency comprises a hybridisation and/or a wash carried out in 0.2xSSC-2xSSC buffer, 0.1% (w/v) SDS at 42°C to 65°C, while a high stringency comprises a hybridisation and/or a wash carried out in 0.1xSSC-0.2xSSC buffer, 0.1% (w/v) SDS at a temperature of at least 55°C. Conditions for hybridisations and washes are well understood by one normally skilled in the art. For the purposes of further clarification only, reference to the parameters affecting hybridisation between nucleic acid molecules is found in pages 20 2.10.8 to 2.10.16. of Ausubel et al. (1987), which is herein incorporated by reference.

In an even more preferred embodiment of the invention, the isolated nucleic acid molecule further comprises a sequence of nucleotides which is at least 40% identical to at least 10 contiguous nucleotides derived from any one or more of SEQ ID Nos:1, 3, 4, 5, 7, 9, 11 or 25 13, or a complementary strand thereof.

Still more preferably, the isolated nucleic acid molecule further comprises a sequence of nucleotides which is at least 40% identical to at least 50 contiguous nucleotides derived from the sequence set forth in any one or more of SEQ ID Nos:1, 3, 4, 5, 7, 9, 11 or 13, or a 30 complementary strand thereof.

The present invention is particularly directed to a nucleic acid molecule which is capable of functioning as a cellulose gene as hereinbefore defined, for example a cellulose synthase gene such as, but not limited to, the *Arabidopsis thaliana*, *Oryza sativa*, wheat, barley, maize, *Brassica ssp.*, *Gossypium hirsutum* or *Eucalyptus ssp.* cellulose synthase genes, amongst others. The subject invention clearly contemplates additional cellulose genes to those specifically described herein which are derived from these plant species.

The invention further contemplates other sources of cellulose genes such as but not limited to, tissues and cultured cells of plant origin. Preferred plant species according to this embodiment include hemp, jute, flax and woody plants including, but not limited to *Pinus ssp.*, *Populus ssp.*, *Picea spp.*, amongst others.

A genetic sequence which encodes or is complementary to a sequence which encodes a polypeptide which is involved in cellulose biosynthesis may correspond to the naturally occurring sequence or may differ by one or more nucleotide substitutions, deletions and/or additions. Accordingly, the present invention extends to cellulose genes and any functional genes, mutants, derivatives, parts, fragments, homologues or analogues thereof or non-functional molecules but which are at least useful as, for example, genetic probes, or primer sequences in the enzymatic or chemical synthesis of said gene, or in the generation of 20 immunologically interactive recombinant molecules.

In a particularly preferred embodiment, the cellulose genetic sequences are employed to identify and isolate similar genes from plant cells, tissues, or organ types of the same species, or from the cells, tissues, or organs of another plant species.

25

According to this embodiment, there is contemplated a method for identifying a related cellulose gene or related cellulose genetic sequence, for example a cellulose synthase or cellulose synthase-like gene, said method comprising contacting genomic DNA, or mRNA, or cDNA with a hybridisation effective amount of a first cellulose genetic sequence 30 comprising any one or more of SEQ ID Nos:1, 3, 4, 5, 7, 9, 11 or 13, or a complementary

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sequence, homologue, analogue or derivative thereof derived from at least 10 contiguous nucleotides of said first sequence, and then detecting said hybridisation.

Preferably, the first genetic sequence comprises at least 50 contiguous nucleotides, even more 5 preferably at least 100 contiguous nucleotides and even more preferably at least 500 contiguous nucleotides, derived from any one or more of SEQ ID Nos:1, 3, 4, 5, 7, 9, 11 or 13, or a complementary strand, homologue, analogue or derivative thereof.

The related cellulose gene or related cellulose genetic sequence may be in a recombinant form, in a virus particle, bacteriophage particle, yeast cell, animal cell, or a plant cell. Preferably, the related cellulose gene or related cellulose genetic sequence is derived from a plant species, such as a monocotyledonous plant or a dicotyledonous plant selected from the list comprising Arabidopsis thaliana, wheat, barley, maize, Brassica ssp., Gossypium hirsutum (cotton), Oryza sativa (rice), Eucalyptus ssp., hemp, jute, flax, and woody plants including, but not limited to Pinus ssp., Populus ssp., Picea spp., amongst others.

More preferably, related cellulose gene or related cellulose genetic sequence is derived from a plant which is useful in the fibre or timber industries, for example Gossypium hirsutum (cotton), hemp, jute, flax, Eucalyptus ssp. or Pinus ssp., amongst others. Alternatively, the related cellulose gene or related cellulose genetic sequence is derived from a plant which is useful in the cereal or starch industry, for example wheat, barley, rice or maize, amongst others.

In a particularly preferred embodiment, the first cellulose genetic sequence is labelled with 25 a reporter molecule capable of giving an identifiable signal (e.g. a radioisotope such as ³²P or ³⁵S or a biotinylated molecule).

An alternative method contemplated in the present invention involves hybridising two nucleic acid "primer molecules" to a nucleic acid "template molecule" which comprises a related 30 cellulose gene or related cellulose genetic sequence or a functional part thereof, wherein the

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first of said primers comprises contiguous nucleotides derived from any one or more of SEQ ID Nos:1, 3, 4, 5, 7, 9, 11 or 13 or a homologue, analogue or derivative thereof and the second of said primers comprises contiguous nucleotides complementary to any one or more of SEQ ID Nos:1, 3, 4, 5, 7, 9, 11 or 13. Specific nucleic acid molecule copies of the template molecule are amplified enzymatically in a polymerase chain reaction, a technique that is well known to one skilled in the art.

In a preferred embodiment, each nucleic acid primer molecule is at least 10 nucleotides in length, more preferably at least 20 nucleotides in length, even more preferably at least 30 nucleotides in length, still more preferably at least 40 nucleotides in length and even still more preferably at least 50 nucleotides in length.

Furthermore, the nucleic acid primer molecules consists of a combination of any of the nucleotides adenine, cytidine, guanine, thymidine, or inosine, or functional analogues or derivatives thereof which are at least capable of being incorporated into a polynucleotide molecule without having an inhibitory effect on the hybridisation of said primer to the template molecule in the environment in which it is used.

Furthermore, one or both of the nucleic acid primer molecules may be contained in an aqueous mixture of other nucleic acid primer molecules, for example a mixture of degenerate primer sequences which vary from each other by one or more nucleotide substitutions or deletions. Alternatively, one or both of the nucleic acid primer molecules may be in a substantially pure form.

25 The nucleic acid template molecule may be in a recombinant form, in a virus particle, bacteriophage particle, yeast cell, animal cell, or a plant cell. Preferably, the nucleic acid

template molecule is derived from a plant cell, tissue or organ, in particular a cell, tissue or organ derived from a plant selected from the list comprising Arabidopsis thaliana, Oryza sativa, wheat, barley, maize, Brassica ssp., Gossypium hirsutum and Eucalyptus ssp., hemp, jute, flax, and woody plants including, but not limited to Pinus ssp., Populus ssp., Picea 5 spp., amongst others.

Those skilled in the art will be aware that there are many known variations of the basic polymerase chain reaction procedure, which may be employed to isolate a related cellulose gene or related cellulose genetic sequence when provided with the nucleotide sequences set 10 forth in any one or more of SEQ ID Nos:1, 3, 4, 5, 7, 9, 11 or 13. Such variations are discussed, for example, in McPherson et al (1991). The present invention extends to the use of all such variations in the isolation of related cellulose genes or related cellulose genetic sequences using the nucleotide sequences embodied by the present invention.

- 15 The isolated nucleic acid molecule according to any of the further embodiments may be cloned into a plasmid or bacteriophage molecule, for example to facilitate the preparation of primer molecules or hybridisation probes or for the production of recombinant gene products. Methods for the production of such recombinant plasmids, cosmids, bacteriophage molecules or other recombinant molecules are well-known to those of ordinary skill in the art and can be accomplished without undue experimentation. Accordingly, the invention further extends to any recombinant plasmid, bacteriophage, cosmid or other recombinant molecule comprising the nucleotide sequence set forth in any one or more of SEQ ID Nos:1, 3, 4, 5, 7, 9, 11 or 13, or a complementary sequence, homologue, analogue or derivative thereof.
- 25 The nucleic acid molecule of the present invention is also useful for developing genetic constructs which express a cellulose genetic sequence, thereby providing for the increased expression of genes involved in cellulose biosynthesis in plants, selected for example from the list comprising Arabidopsis thaliana, Oryza sativa, wheat, barley, maize, Brassica ssp., Gossypium hirsutum and Eucalyptus ssp., hemp, jute, flax, and woody plants including, but 30 not limited to Pinus ssp., Populus ssp., Picea spp., amongst others. The present invention

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particularly contemplates the modification of cellulose biosynthesis in cotton, hemp, jute, flax, Eucalyptus ssp. and Pinus ssp., amongst others.

The present inventors have discovered that the genetic sequences disclosed herein are capable of being used to modify the level of non-crystalline β-1,4,-glucan, in addition to altering cellulose levels when expressed, particularly when expressed in plants cells. In particular, the Arabidopsis thaliana rsw1 mutant has increased levels of non-crystalline β-1,4,-glucan, when grown at 31°C, compared to wild-type plants, grown under identical conditions. The expression of a genetic sequence described herein in the antisense orientation in transgenic plants grown at only 21°C is shown to reproduce many aspects of the rsw1 mutant phenotype.

Accordingly, the present invention clearly extends to the modification of non-crystalline β-1,4,-glucan biosynthesis in plants, selected for example from the list comprising Arabidopsis thaliana, Oryza sativa, wheat, barley, maize, Brassica ssp., Gossypium hirsutum and 15 Eucalyptus ssp., hemp, jute, flax, and woody plants including, but not limited to Pinus ssp., Populus ssp., Picea spp., amongst others. The present invention particularly contemplates the modification of non-crystalline β-1,4,-glucan biosynthesis in cotton, hemp, jute, flax, Eucalyptus ssp. and Pinus ssp., amongst others.

20 The present invention further extends to the production and use of non-crystalline β -1,4-glucan and to the use of the glucan to modify the properties of plant cell walls or cotton fibres or wood fibres. Such modified properties are described herein (Example 13).

The inventors have discovered that the *rsw*1 mutant has altered carbon partitioning compared to wild-type plants, resulting in significantly higher starch levels therein. The isolated nucleic acid molecules provided herein are further useful for altering the carbon partitioning in a cell. In particular, the present invention contemplates increased starch production in transgenic plants expressing the nucleic acid molecule of the invention in the antisense orientation or alterntively, expressing a ribozyme or co-suppression molecule comprising the nucleic acid sequence of the invention.

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The invention further contemplates reduced starch and/or non-crystalline β -1.4-glucan product in transgenic plants expressing the nucleic acid molecule of the invention in the sense orientation such that cellulose production is increased therein.

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5 Wherein it is desired to increase cellulose production in a plant cell, the coding region of a cellulose gene is placed operably behind a promoter, in the sense orientation, such that a cellulose gene product is capable of being expressed under the control of said promoter sequence. In a preferred embodiment, the cellulose genetic sequence is a cellulose synthase genomic sequence, cDNA molecule or protein-coding sequence.

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In a particularly preferred embodiment, the cellulose genetic sequence comprises a sequence of nucleotides substantially the same as the sequence set forth in any one or more of SEQ ID Nos:1, 3, 4, 5, 7, 9, 11 or 13 or a homologue, analogue or derivative thereof.

- Wherein it is desirable to reduce the content of cellulose or to increase the content of non-crystalline β-1,4-glucan, the nucleic acid molecule of the present invention is expressed in the antisense orientation under the control of a suitable promoter. Additionally, the nucleic acid molecule of the invention is also useful for developing ribozyme molecules, or in cosuppression of a cellulose gene. The expression of an antisense, ribozyme or co-suppression molecule comprising a cellulose gene, in a cell such as a plant cell, fungal cell, insect cell. animal cell, yeast cell or bacterial cell, may also increase the solubility, digestibility or extractability of metabolites from plant tissues or alternatively, or increase the availability of carbon as a precursor for any secondary metabolite other than cellulose (e.g. starch or sucrose). By targeting the endogenous cellulose gene, expression is diminished, reduced or otherwise lowered to a level that results in reduced deposition of cellulose in the primary or secondary cell walls of the plant cell, fungal cell, insect cell. animal cell, yeast cell or bacterial cell, and more particularly, a plant cell. Additionally, or alternatively, the content of non-crystalline β-1,4-glucan is increased in such cells.
- 30 Co-suppression is the reduction in expression of an endogenous gene that occurs when one

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or more copies of said gene, or one or more copies of a substantially similar gene are introduced into the cell. The present invention also extends to the use of co-suppression to inhibit the expression of a gene which encodes a cellulose gene product, such as but not limited to cellulose synthase. Preferably, the co-suppression molecule of the present invention targets a plant mRNA molecule which encodes a cellulose synthase enzyme, for example a plant, fungus, or bacterial cellulose synthase mRNA, and more preferably a plant mRNA derived from Arabidopsis thaliana, Oryza sativa, wheat, barley, maize, Brassica ssp., Gossypium hirsutum and Eucalyptus ssp., hemp, jute, flax, or a woody plant such as Pinus ssp., Populus ssp., or Picea spp., amongst others.

10

In a particularly preferred embodiment, the gene which is targeted by a co-suppression molecule, comprises a sequence of nucleotides set forth in any one or more of SEQ ID Nos:1, 3, 4, 5, 7, 9, 11 or 13, or a complement, homologue, analogue or derivative thereof.

- 15 In the context of the present invention, an antisense molecule is an RNA molecule which is transcribed from the complementary strand of a nuclear gene to that which is normally transcribed to produce a "sense" mRNA molecule capable of being translated into a polypeptide component of the cellulose biosynthetic pathway. The antisense molecule is therefore complementary to the mRNA transcribed from a sense cellulose gene or a part thereof. Although not limiting the mode of action of the antisense molecules of the present invention to any specific mechanism, the antisense RNA molecule possesses the capacity to form a double-stranded mRNA by base pairing with the sense mRNA, which may prevent translation of the sense mRNA and subsequent synthesis of a polypeptide gene product.
- 25 Preferably, the antisense molecule of the present invention targets a plant mRNA molecule which encodes a cellulose gene product, for example cellulose synthase. Preferably, the antisense molecule of the present invention targets a plant mRNA molecule which encodes a cellulose synthase enzyme, for example a plant mRNA derived from Arabidopsis thaliana, Oryza sativa, wheat, barley, maize, Brassica ssp., Gossypium hirsutum and Eucalyptus ssp., 30 hemp, jute, flax, or a woody plant such as Pinus ssp., Populus ssp., or Picea spp., amongst

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others.

In a particularly preferred embodiment, the antisense molecule of the invention targets an mRNA molecule encoded by any one or more of SEQ ID Nos:1, 3, 4, 5, 7, 9, 11 or 13, or 5 a homologue, analogue or derivative thereof.

Ribozymes are synthetic RNA molecules which comprise a hybridising region complementary to two regions, each of at least 5 contiguous nucleotide bases in the target sense mRNA. In addition, ribozymes possess highly specific endoribonuclease activity, which autocatalytically cleaves the target sense mRNA. A complete description of the function of ribozymes is presented by Haseloff and Gerlach (1988) and contained in International Patent Application No. WO89/05852.

The present invention extends to ribozyme which target a sense mRNA encoding a cellulose gene product, thereby hybridising to said sense mRNA and cleaving it, such that it is no longer capable of being translated to synthesise a functional polypeptide product. Preferably, the ribozyme molecule of the present invention targets a plant mRNA molecule which encodes a cellulose synthase enzyme, for example a plant mRNA derived from Arabidopsis thaliana, Gossypium hirsutum (cotton), Oryza sativa (rice), Eucalyptus ssp., hemp, jute, flax, or a woody plant such as Pinus ssp., Populus ssp., or Picea spp., amongst others.

In a particularly preferred embodiment, the ribozyme molecule will target an mRNA encoded by any one or more of SEQ ID Nos:1, 3, 4, 5, 7, 9, 11 or 13, or a homologue, analogue or derivative thereof.

25

According to this embodiment, the present invention provides a ribozyme or antisense molecule comprising at least 5 contiguous nucleotide bases derived from any one or more of SEQ ID Nos:1, 3, 4, 5, 7, 9, 11 or 13, or a complementary nucleotide sequence or a homologue, analogue or derivative thereof, wherein said antisense or ribozyme molecule is 30 able to form a hydrogen-bonded complex with a sense mRNA encoding a cellulose gene

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product to reduce translation thereof.

In a preferred embodiment, the antisense or ribozyme molecule comprises at least 10 to 20 contiguous nucleotides derived from any one or more of SEQ ID Nos:1, 3, 4, 5, 7, 9, 11 or 13, or a complementary nucleotide sequence or a homologue, analogue or derivative thereof. Although the preferred antisense and/or ribozyme molecules hybridise to at least about 10 to 20 nucleotides of the target molecule, the present invention extends to molecules capable of hybridising to at least about 50-100 nucleotide bases in length, or a molecule capable of hybridising to a full-length or substantially full-length mRNA encoded by a cellulose gene, 10 such as a cellulose synthase gene.

Those skilled in the art will be aware of the necessary conditions, if any, for selecting or preparing the antisense or ribozyme molecules of the invention.

- 15 It is understood in the art that certain modifications, including nucleotide substitutions amongst others, may be made to the antisense and/or ribozyme molecules of the present invention, without destroying the efficacy of said molecules in inhibiting the expression of a gene encoding a cellulose gene product such as cellulose synthase. It is therefore within the scope of the present invention to include any nucleotide sequence variants, homologues, analogues, or fragments of the said gene encoding same, the only requirement being that said nucleotide sequence variant, when transcribed, produces an antisense and/or ribozyme molecule which is capable of hybridising to a sense mRNA molecule which encodes a cellulose gene product.
- DNA sequence to which it hybridises, thereby altering the form and/or function of the endogenous gene and the subsequent phenotype of the cell. According to this embodiment, at least a part of the DNA sequence defined by any one or more of SEQ ID Nos:1, 3, 4, 5, 7, 9, 11 or 13, or a related cellulose genetic sequence, may be introduced into target cells containing an endogenous cellulose gene, thereby replacing said endogenous cellulose gene.

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According to this embodiment, the polypeptide product of said cellulose genetic sequence possesses different catalytic activity and/or expression characteristics, producing in turn modified cellulose deposition in the target cell. In a particularly preferred embodiment of the invention, the endogenous cellulose gene of a plant is replaced with a gene which is merely capable of producing non-crystalline β-1,4-glucan polymers or alternatively which is capable of producing a modified cellulose having properties similar to synthetic fibres such as rayon, in which the β-1,4-glucan polymers are arranged in an antiparallel configuration relative to one another.

10 The present invention extends to genetic constructs designed to facilitate expression of a cellulose genetic sequence which is identical, or complementary to the sequence set forth in any one or more of SEQ ID Nos:1, 3, 4, 5, 7, 9, 11 or 13, or a functional derivative, part, homologue, or analogue thereof, or a genetic construct designed to facilitate expression of a sense molecule, an antisense molecule, ribozyme molecule, co-suppression molecule, or 15 gene targeting molecule containing said genetic sequence.

The said genetic construct of the present invention comprises the foregoing sense, antisense, or ribozyme, or co-suppression nucleic acid molecule, or gene-targeting molecule, placed operably under the control of a promoter sequence capable of regulating the expression of the said nucleic acid molecule in a prokaryotic or eukaryotic cell, preferably a plant cell. The said genetic construct optionally comprises, in addition to a promoter and sense, or antisense, or ribozyme, or co-suppression, or gene-targeting nucleic acid molecule, a terminator sequence.

25 The term "terminator" refers to a DNA sequence at the end of a transcriptional unit which signals termination of transcription. Terminators are 3'-non-translated DNA sequences containing a polyadenylation signal, which facilitates the addition of polyadenylate sequences to the 3'-end of a primary transcript. Terminators active in plant cells are known and described in the literature. They may be isolated from bacteria, fungi, viruses, animals 30 and/or plants. Examples of terminators particularly suitable for use in the genetic constructs

of the present invention include the nopaline synthase (NOS) gene terminator of Agrobacterium tumefaciens, the terminator of the Cauliflower mosaic virus (CaMV) 35S gene, and the zein gene terminator from Zea mays.

- 5 Reference herein to a "promoter" is to be taken in its broadest context and includes the transcriptional regulatory sequences of a classical genomic gene, including the TATA box which is required for accurate transcription initiation, with or without a CCAAT box sequence and additional regulatory elements (i.e. upstream activating sequences, enhancers and silencers) which alter gene expression in response to developmental and/or external stimuli, or in a tissue-specific manner. A promoter is usually, but not necessarily, positioned upstream or 5', of a structural gene, the expression of which it regulates. Furthermore, the regulatory elements comprising a promoter are usually positioned within 2 kb of the start site of transcription of the gene.
- In the present context, the term "promoter" is also used to describe a synthetic or fusion molecule, or derivative which confers, activates or enhances expression of said sense, antisense, or ribozyme, or co-suppression nucleic acid molecule, in a plant cell. Preferred promoters may contain additional copies of one or more specific regulatory elements, to further enhance expression of a sense antisense, ribozyme or co-suppression molecule and/or to alter the spatial expression and/or temporal expression of said sense or antisense, or ribozyme, or co-suppression, or gene-targeting molecule. For example, regulatory elements which confer copper inducibility may be placed adjacent to a heterologous promoter sequence driving expression of a sense, or antisense, or ribozyme, or co-suppression, or gene-targeting molecule, thereby conferring copper inducibility on the expression of said molecule.

25

Placing a sense or ribozyme, or antisense, or co-suppression, or gene-targeting molecule under the regulatory control of a promoter sequence means positioning the said molecule such that expression is controlled by the promoter sequence. Promoters are generally positioned 5' (upstream) to the genes that they control. In the construction of heterologous promoter/structural gene combinations it is generally preferred to position the promoter at a

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distance from the gene transcription start site that is approximately the same as the distance between that promoter and the gene it controls in its natural setting, i.e., the gene from which the promoter is derived. As is known in the art, some variation in this distance can be accommodated without loss of promoter function. Similarly, the preferred positioning of a regulatory sequence element with respect to a heterologous gene to be placed under its control is defined by the positioning of the element in its natural setting, i.e., the genes from which it is derived. Again, as is known in the art, some variation in this distance can also occur.

Examples of promoters suitable for use in genetic constructs of the present invention include viral, fungal, bacterial, animal and plant derived promoters capable of functioning in prokaryotic or eukaryotic cells. Preferred promoters are those capable of regulating the expression of the subject cellulose genes of the innvention in plants cells, fungal cells, insect cells, yeast cells, animal cells or bacterial cells, amongst others. Particularly preferred promoters are capable of regulating expression of the subject nucleic acid molecules in plant cells. The promoter may regulate the expression of the said molecule constitutively, or differentially with respect to the tissue in which expression occurs or, with respect to the developmental stage at which expression occurs, or in response to external stimuli such as physiological stresses, or plant pathogens, or metal ions, amongst others. Preferably, the promoter is capable of regulating expression of a sense, or ribozyme, or antisense, or co20 suppression molecule or gene targeting, in a plant cell. Examples of preferred promoters include the CaMV 35S promoter, NOS promoter, octopine synthase (OCS) promoter and the like.

In a most preferred embodiment, the promoter is capable of expression in any plant cell, such as, but not limited to a plant selected from the list comprising Arabidopsis thaliana, Oryza sativa, wheat, barley, maize, Brassica ssp., Gossypium hirsutum and Eucalyptus ssp., hemp, jute, flax, and woody plants including, but not limited to Pinus ssp., Populus ssp., Picea spp., amongst others.

30 In a particularly preferred embodiment, the promoter may be derived from a genomic clone

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encoding a cellulose gene product, in particular the promoter contained in the sequence set forth in SEQ ID NO:3 or SEQ ID NO:4. Preferably, the promoter sequence comprises nucleotide 1 to about 1900 of SEQ ID NO:3 or nucleotides 1 to about 700 of SEQ ID NO:4 or a homologue, analogue or derivative capable of hybridizing thereto under at least low 5 stringency conditions.

Optionally, the genetic construct of the present invention further comprises a terminator sequence.

10 In an exemplification of this embodiment, there is provided a binary genetic construct comprising the isolated nucleotide sequence of nucleotides set forth in SEQ ID NO:3. There is also provided a genetic construct comprising the isolated nucleotide sequence of nucleotides set forth in SEQ ID NO:1, in the antisense orientation, placed operably in connection with the CaMV 35S promoter.

15

In the present context, the term "in operable connection with" means that expression of the isolated nucleotide sequence is under the control of the promoter sequence with which it is connected, regardless of the relative physical distance of the sequences from each other or their relative orientation with respect to each other.

20

An alternative embodiment of the invention is directed to a genetic construct comprising a promoter or functional derivative, part, fragment, homologue, or analogue thereof, which is capable of directing the expression of a polypeptide early in the development of a plant cell at a stage when the cell wall is developing, such as during cell expansion or during cell division. In a particularly preferred embodiment, the promoter is contained in the sequence set forth in SEQ ID NO:3 or SEQ ID NO:4. Preferably, the promoter sequence comprises nucleotide 1 to about 1900 of SEQ ID NO:3 or nucleotides 1 to about 700 of SEQ ID NO:4 or a homologue, analogue or derivative capable of hybridizing thereto under at least low stringency conditions.

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The polypeptide may be a reporter molecule which is encoded by a gene such as the bacterial β-glucuronidase gene or chloramphenicol acetyltransferase gene or alternatively, the firefly luciferase gene. Alternatively, the polypeptide may be encoded by a gene which is capable of producing a modified cellulose in the plant cell when placed in combination with the normal complement of cellulose genes which are expressible therein, for example it may be a cellulose-like gene obtained from a bacterial or fungal source or a cellulose gene obtained from a plant source.

The genetic constructs of the present invention are particularly useful in the production of crop plants with altered cellulose content or structure. In particular, the rate of cellulose deposition may be reduced leading to a reduction in the total cellulose content of plants by transferring one or more of the antisense, ribozyme or co-suppression molecules described supra into a plant or alternatively, the same or similar end-result may be achieved by replacing an endogenous cellulose gene with an inactive or modified cellulose gene using gene-targeting approaches. The benefits to be derived from reducing cellulose content in plants are especially apparent in food and fodder crops such as, but not limited to maize, wheat, barley, rye, rice, barley, millet or sorghum, amongst others where improved digestibility of said crop is desired. The foregoing antisense, ribozyme or co-suppression molecules are also useful in producing plants with altered carbon partitioning such that increased carbon is available for growth, rather than deposited in the form of cellulose.

Alternatively, the introduction to plants of additional copies of a cellulose gene in the 'sense' orientation and under the control of a strong promoter is useful for the production of plants with increased cellulose content or more rapid rates of cellulose biosynthesis. Accordingly, such plants may exhibit a range of desired traits including, but not limited to modified strength and/or shape and/or properties of fibres, cell and plants, increased protection against chemical, physical or environmental stresses such as dehydration, heavy metals (e.g. cadmium) cold, heat or wind, increased resistance to attack by pathogens such as insects, nematodes and the like which physically penetrate the cell wall barrier during invasion/infection of the plant.

Alternatively, the production of plants with altered physical properties is made possible by the introduction thereto of altered cellulose gene(s). Such plants may produce β-1,4-glucan which is either non-crystalline or shows altered crystallinity. Such plants may also exhibit a range of desired traits including but not limited to, altered dietary fibre content, altered digestibility and degradability or producing plants with altered extractability properties.

Furthermore, genetic constructs comprising a plant cellulose gene in the 'sense' orientation may be used to complement the existing range of cellulose genes present in a plant, thereby altering the composition or timing of deposition of cellulose deposited in the cell wall of said plant. In a preferred embodiment, the cellulose gene from one plant species or a β-1,4-glucan synthase gene from a non-plant species is used to transform a plant of a different species, thereby introducing novel cellulose biosynthetic metabolism to the second-mentioned plant species.

- In a related embodiment, a recombinant fusion polypeptide may be produced containing the active site from one cellulose gene product fused to another cellulose gene product, wherein said fusion polypeptide exhibits novel catalytic properties compared to either 'parent' polypeptide from which it is derived. Such fusion polypeptides may be produced by conventional recombinant DNA techniques known to those skilled in the art, either by introducing a recombinant DNA capable of expressing the entire fusion polypeptide into said plant or alternatively, by a gene-targeting approach in which recombination at the DNA level occurs in vivo and the resultant gene is capable of expressing a recombinant fusion polypeptide.
- 25 The present invention extends to all transgenic methods and products described *supra*, including genetic constructs.

The recombinant DNA molecule carrying the sense, antisense, ribozyme or co-suppression molecule of the present invention and/or genetic construct comprising the same, may be 30 introduced into plant tissue, thereby producing a "transgenic plant", by various techniques

known to those skilled in the art. The technique used for a given plant species or specific type of plant tissue depends on the known successful techniques. Means for introducing recombinant DNA into plant tissue include, but are not limited to, transformation (Paszkowski et al., 1984), electroporation (Fromm et al., 1985), or microinjection of the 5 DNA (Crossway et al., 1986), or T-DNA-mediated transfer from Agrobacterium to the plant tissue. Representative T-DNA vector systems are described in the following references: An et al. (1985); Herrera-Estrella et al. (1983a,b); Herrera-Estrella et al. (1985). Once introduced into the plant tissue, the expression of the introduced gene may be assayed in a transient expression system, or it may be determined after selection for stable integration within the plant genome. Techniques are known for the in vitro culture of plant tissue, and in a number of cases, for regeneration into whole plants. Procedures for transferring the introduced gene from the originally transformed plant into commercially useful cultivars are known to those skilled in the art.

15 A still further aspect of the present invention extends to a transgenic plant such as a crop plant, carrying the foregoing sense, antisense, ribozyme, co-suppression, or gene-targeting molecule and/or genetic constructs comprising the same. Preferably, the transgenic plant is one or more of the following: Arabidopsis thaliana, Oryza sativa, wheat, barley, maize, Brassica ssp., Gossypium hirsutum and Eucalyptus ssp., hemp, jute, flax, Pinus ssp., 20 Populus ssp., or Picea spp. Additional species are not excluded.

The present invention further extends to the progeny of said transgenic plant.

Yet another aspect of the present invention provides for the expression of the subject genetic sequence in a suitable host (e.g. a prokaryote or eukaryote) to produce full length or non-full length recombinant cellulose gene products.

Hereinafter the term "cellulose gene product" shall be taken to refer to a recombinant product of a cellulose gene as hereinbefore defined. Accordingly, the term "cellulose gene product" includes a polypeptide product of any gene involved in the cellulose biosynthetic pathway in

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plants, such as, but not limited to a cellulose synthase gene product.

Preferably, the recombinant cellulose gene product comprises an amino acid sequence having the catalytic activity of a cellulose synthase polypeptide or a functional mutant, derivative part, fragment, or analogue thereof.

In a particularly preferred embodiment of the invention, the recombinant cellulose gene product comprises a sequence or amino acids that is at least 40% identical to any one or more of SEQ ID Nos:2, 6, 8, 10, 12 or 14, or a homologue, analogue or derivative thereof.

10

Single and three-letter abbreviations used for amino acid residues contained in the specification are provided in Table 1.

In the present context, "homologues" of an amino acid sequence refer to those polypeptides, enzymes or proteins which have a similar catalytic activity to the amino acid sequences described herein, notwithstanding any amino acid substitutions, additions or deletions thereto. A homologue may be isolated or derived from the same or another plant species as the species from which the polypeptides of the invention are derived.

20 "Analogues" encompass polypeptides of the invention notwithstanding the occurrence of any non-naturally occurring amino acid analogues therein.

"Derivatives" include modified peptides in which ligands are attached to one or more of the amino acid residues contained therein, such as carbohydrates, enzymes, proteins, polypeptides or reporter molecules such as radionuclides or fluorescent compounds. Glycosylated, fluorescent, acylated or alkylated forms of the subject peptides are particularly contemplated by the present invention. Additionally, derivatives of an amino acid sequence described herein which comprises fragments or parts of the subject amino acid sequences are within the scope of the invention, as are homopolymers or heteropolymers comprising two or more 30 copies of the subject polypeptides. Procedures for derivatizing peptides are well-known in the

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art.

TABLE 1

| | Amino Acid | Three-letter | One-letter |
|----|----------------|--------------|--------------|
| _ | | Abbreviation | Symbol |
| 5 | Alanine | Ala | Α |
| | Arginine | Arg | R |
| | Asparagine | Asn | N |
| | Aspartic acid | Asp | D |
| | Cysteine | Cys | C |
| 10 | D-alanine | Dal | x |
| | Glutamine | Gln | Q |
| | Glutamic acid | Glu | E |
| | Glycine | Gly | G |
| | Histidine | His | Н |
| 15 | Isoleucine | Ile | I |
| | Leucine | Leu | L |
| | Lysine | Lys | K |
| | Methionine | Met | M |
| | Phenylalanine | Phe | F |
| 20 | Proline | Pro | P |
| | Serine | Ser | S |
| | Threonine | Thr | T |
| | Tryptophan | Trp | \mathbf{w} |
| | Tryosine | Туг | Y |
| 25 | Valine | Val | v |
| | Any amino acid | Xaa | X |

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Substitutions encompass amino acid alterations in which an amino acid is replaced with a different naturally-occurring or a non-conventional amino acid residue. Such substitutions may be classified as "conservative". in which an amino acid residue contained in a cellulose gene product is replaced with another naturally-occurring amino acid of similar character, for example Gly↔Ala, Val↔Ile↔Leu, Asp↔Glu, Lys↔Arg, Asn↔Gln or Phe↔Trp↔Tyr.

Substitutions encompassed by the present invention may also be "non-conservative", in which an amino acid residue which is present in a cellulose gene product described herein is substituted with an amino acid with different properties, such as a naturally-occurring amino acid from a different group (eg. substituted a charged or hydrophobic amino acid with alanine), or alternatively, in which a naturally-occurring amino acid is substituted with a non-conventional amino acid.

Non-conventional amino acids encompassed by the invention include, but are not limited to 15 those listed in Table 2.

Amino acid substitutions are typically of single residues, but may be of multiple residues, either clustered or dispersed.

20 Amino acid deletions will usually be of the order of about 1-10 amino acid residues, while insertions may be of any length. Deletions and insertions may be made to the N-terminus, the C-terminus or be internal deletions or insertions. Generally, insertions within the amino acid sequence will be smaller than amino- or carboxy-terminal fusions and of the order of 1-4 amino acid residues.

25

A homologue, analogue or derivative of a cellulose gene product as referred to herein may readily be made using peptide synthetic techniques well-known in the art, such as solid phase peptide synthesis and the like, or by recombinant DNA manipulations. Techniques for making substituent mutations at pre-determined sites using recombinant DNA technology, for 30 example by M13 mutagenesis, are also well-known. The manipulation of nucleic acid

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molecules to produce variant peptides, polypeptides or proteins which manifest as substitutions, insertions or deletions are well-known in the art.

The cellulose gene products described herein may be derivatized further by the inclusion or 5 attachment thereto of a protective group which prevents, inhibits or slows proteolytic or cellular degradative processes. Such derivatization may be useful where the half-life of the subject polypeptide is required to be extended, for ample to increase the amount of cellulose produced in a primary or secondary cell wall of a plant cell or alternatively, to increase the amount of protein produced in a bacterial or eukaryotic expression system. Examples of 10 chemical groups suitable for this purpose include, but are not limited to, any of the nonconventional amino acid residues listed in Table 2, in particular a D-stereoisomer or a methylated form of a naturally-occurring amino acid listed in Table 1. Additional chemical groups which are useful for this purpose are selected from the list comprising aryl or heterocyclic N-acyl substituents, polyalkylene oxide moieties, desulphatohirudin muteins, 15 alpha-muteins, alpha-aminophosphonic acids, water-soluble polymer groups such as polyethylene glycol attached to sugar residues using hydrazone or oxime groups, benzodiazepine dione derivatives, glycosyl groups such as beta-glycosylamine or a derivative thereof, isocyanate conjugated to a polyol functional group or polyoxyethylene polyol capped with diisocyanate, amongst others. Similarly, a cellulose gene product or a homologue, 20 analogue or derivative thereof may be cross-linked or fused to itself or to a protease inhibitor peptide, to reduce susceptibility of said molecule to proteolysis.

TABLE 2

| Non-conventional amino acid | Code | Non-conventional amino acid | Code |
|-----------------------------|---------|-----------------------------|----------------|
| 5 | Abu | L-N-methylalanine | Nmala |
| α-aminobutyric acid | | L-N-methylarginine | Nmarg |
| α-amino-α-methylbutyrate | Mgabu | • 5 | Nmasn |
| aminocyclopropane- | Срго | L-N-methylasparagine | Nmasp |
| carboxylate | A 16. | L-N-methylaspartic acid | Nmcys |
| 0 aminoisobutyric acid | Aib | L-N-methylcysteine | ¥ |
| aminonorbornyl- | Norb | L-N-methylglutamine | Nmgln |
| carboxylate | Observe | L-N-methylglutamic acid | Nmglu Nmhis |
| cyclohexylalanine | Chexa | L-N-methylhistidine | Nmile |
| cyclopentylalanine | Cpen | L-N-methylisolleucine | Nmleu |
| 5 D-alanine | Dal | L-N-methylleucine | |
| D-arginine | Darg | L-N-methyllysine | Nmlys |
| D-aspartic acid | Dasp | L-N-methylmethionine | Nmmet |
| D-cysteine | Dcys | L-N-methylnorleucine | Nmnle |
| D-glutamine | Dgln | L-N-methylnorvaline | Nmnva |
| O D-glutamic acid | Dglu | L-N-methylornithine | Nmorn |
| D-histidine | Dhis | L-N-methylphenylalanine | Nmphe |
| D-isoleucine | Dile | L-N-methylproline | Nmpro |
| D-leucine | Dleu | L-N-methylserine | Nmser |
| D-lysine | Dlys | L-N-methylthreonine | Nmthr |
| 25 D-methionine | Dmet | L-N-methyltryptophan | Nmtrp |
| D-ornithine | Dorn | L-N-methyltyrosine | Nmtyr |
| D-phenylalanine | Dphe | L-N-methylvaline | Nmval |
| D-proline | Dpro | L-N-methylethylglycine | Nmetg |
| D-serine | Dser | L-N-methyl-t-butylglycine | Nmtbug |
| 30 D-threonine | Dthr | L-norleucine | Nle |

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| | | ъ. | T | Maria |
|----|------------------------------|--------|--|--------|
| | D-tryptophan | Dtrp | L-norvaline | Nva |
| | D-tyrosine | Dtyr | α-methyl-aminoisobutyrate | Maib |
| | D-valine | Dval | α -methyl- γ -aminobutyrate | Mgabu |
| | D-α-methylalanine | Dmala | α-methylcyclohexylalanine | Mchexa |
| 5 | D-α-methylarginine | Dmarg | α-methylcylcopentylalanine | Mcpen |
| | $D-\alpha$ -methylasparagine | Dmasn | α -methyl- α -napthylalanine | Manap |
| | D-α-methylaspartate | Dmasp | α -methylpenicillamine | Mpen |
| | D-α-methylcysteine | Dmcys | N-(4-aminobutyl)glycine | Nglu |
| | D-α-methylglutamine | Dmgln | N-(2-aminoethyl)glycine | Naeg |
| 10 | D-α-methylhistidine | Dmhis | N-(3-aminopropyl)glycine | Norn |
| | D-α-methylisoleucine | Dmile | N-amino-α-methylbutyrate | Nmaabu |
| | D-α-methylleucine | Dmleu | α-napthylalanine | Anap |
| | D-α-methyllysine | Dmlys | N-benzylglycine | Nphe |
| | D-α-methylmethionine | Dmmet | N-(2-carbamylethyl)glycine | Ngln |
| 15 | D-α-methylornithine | Dmorn | N-(carbamylmethyl)glycine | Nasn |
| | D-α-methylphenylalanine | Dmphe | N-(2-carboxyethyl)glycine | Nglu |
| | D-α-methylproline | Dmpro | N-(carboxymethyl)glycine | Nasp |
| | D-α-methylserine | Dmser | N-cyclobutylglycine | Ncbut |
| | D-α-methylthreonine | Dmthr | N-cycloheptylglycine | Nchep |
| 20 | D-α-methyltryptophan | Dmtrp | N-cyclohexylglycine | Nchex |
| | D-α-methyltyrosine | Dmty | N-cyclodecylglycine | Ncdec |
| | D-α-methylvaline | Dmval | N-cylcododecylglycine | Ncdod |
| | D-N-methylalanine | Dnmala | N-cyclooctylglycine | Ncoct |
| | D-N-methylarginine | Dnmarg | N-cyclopropylglycine | Ncpro |
| 25 | D-N-methylasparagine | Dnmasn | N-cycloundecylglycine | Ncund |
| | D-N-methylaspartate | Dnmasp | N-(2,2-diphenylethyl)glycine | Nbhm |
| | D-N-methylcysteine | Dnmcys | N-(3,3-diphenylpropyl)glycine | Nbhe |
| | D-N-methylglutamine | Dnmgln | N-(3-guanidinopropyl)glycine | Narg |
| | D-N-methylglutamate | Dnmglu | N-(1-hydroxyethyl)glycine | Nthr |
| 30 | D-N-methylhistidine | Dnmhis | N-(hydroxyethyl))glycine | Nser |
| | | | | |

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| | D-N-methylisoleucine | Dnmile | N-(imidazolylethyl))glycine | Nhis |
|----|---------------------------|---------|------------------------------|--------|
| | D-N-methylleucine | Dnmleu | N-(3-indolylyethyl)glycine | Nhtrp |
| | D-N-methyllysine | Dnmlys | N-methyl-γ-aminobutyrate | Nmgabu |
| | N-methylcyclohexylalanine | Nmchexa | D-N-methylmethionine | Dnmmet |
| 5 | D-N-methylornithine | Dnmorn | N-methylcyclopentylalanine | Nmcpen |
| | N-methylglycine | Nala | D-N-methylphenylalanine | Dnmphe |
| | N-methylaminoisobutyrate | Nmaib | D-N-methylproline | Dnmpro |
| | N-(1-methylpropyl)glycine | Nile | D-N-methylserine | Dnmser |
| | N-(2-methylpropyl)glycine | Nleu | D-N-methylthreonine | Dnmthr |
| 10 | D-N-methyltryptophan | Dnmtrp | N-(1-methylethyl)glycine | Nval |
| | D-N-methyltyrosine | Dnmtyr | N-methyla-napthylalanine | Nmanap |
| | D-N-methylvaline | Dnmval | N-methylpenicillamine | Nmpen |
| | γ-aminobutyric acid | Gabu | N-(p-hydroxyphenyl)glycine | Nhtyr |
| | L-t-butylglycine | Tbug | N-(thiomethyl)glycine | Ncys |
| 15 | L-ethylglycine | Etg | penicillamine | Pen |
| | L-homophenylalanine | Hphe | L-α-methylalanine | Mala |
| | L-α-methylarginine | Marg | L-α-methylasparagine | Masn |
| | L-α-methylaspartate | Masp | L-α-methyl-t-butylglycine | Mtbug |
| | L-α-methylcysteine | Mcys | L-methylethylglycine | Metg |
| 20 | L-α-methylglutamine | Mgln | L-α-methylglutamate | Mglu |
| | L-α-methylhistidine | Mhis | L-α-methylhomophenylalanine | Mhphe |
| | L-α-methylisoleucine | Mile | N-(2-methylthioethyl)glycine | Nmet |
| | L-α-methylleucine | Mleu | L-a-methyllysine | Mlys |
| | L-α-methylmethionine | Mmet | L-a-methylnorleucine | Mnle |
| 25 | L-α-methylnorvaline | Mnva | L-a-methylornithine | Morn |
| | L-α-methylphenylalanine | Mphe | L-a-methylproline | Mpro |
| | L-α-methylserine | Mser | L-a-methylthreonine | Mthr |
| | L-α-methyltryptophan | Mtrp | L-a-methyltyrosine | Mtyr |
| | L-α-methylvaline | Mval | L-N-methylhomophenylalanine | Nmhphe |
| | | | | |

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N-(N-(2.2-diphenylethyl) Nnbhm N-(N-(3,3-diphenylpropyl) Nnbhe
carbamylmethyl)glycine carbamylmethyl)glycine
1-carboxy-1-(2,2-diphenyl- Nmbc
ethylamino)cyclopropane

In an alternative embodiment of the invention, the recombinant cellulose gene product is characterised by at least one functional β -glycosyl transferase domain contained therein.

10

The term "β-glycosyl transferase domain" as used herein refers to a sequence of amino acids which is highly conserved in different processive enzymes belonging to the class of glycosyl transferase enzymes (Saxena et al., 1995), for example the bacterial β-1,4-glycosyl transferase enzymes and plant cellulose synthase enzymes amongst others, wherein said domain possesses a putative function in contributing to or maintaining the overall catalytic activity, substrate specificity or substrate binding of an enzyme in said enzyme class. The β-glycosyl transferase domain is recognisable by the occurrence of certain amino acid residues at particular locations in a polypeptide sequence, however there is no stretch of contiguous amino acid residues comprised therein.

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30

As a consequence of the lack of contiguity in a β-glycosyl transferase domain, it is not a straightforward matter to isolate a cellulose gene by taking advantage of the presence of a β-glycosyl transferase domain in the polypeptide encoded by said gene. For example, the β-glycosyl transferase domain would not be easily utilisable as a probe to facilitate the rapid isolation of all β-glycosyl transferase genetic sequences from a particular organism and then to isolate from those genetic sequences a cellulose gene such as cellulose synthase.

In a preferred embodiment, the present invention provides an isolated polypeptide which:

(i)contains at least one structural β-glycosyl transferase domain as hereinbefore defined; and

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- (ii) has at least 40% amino acid sequence similarity to at least 20 contiguous amino acid residues set forth in any one or more of SEQ ID Nos:2, 6, 8, 10, 12 or 14, or a homologue, analogue or derivative thereof.
- 5 More preferably, the polypeptide of the invention is at least 40% identical to at least 50 contiguous amino acid residues, even more preferably at least 100 amino acid residues of any one or more of SEQ ID Nos:2, 6, 8, 10, 12 or 14, or a homologue, analogue or derivative thereof.
- In a particularly preferred embodiment, the percentage similarity to any one or more of SEQ ID Nos:2, 6, 8, 10, 12 or 14 is at least 50-60%, more preferably at least 65-70%, even more preferably at least 75-80% and even more preferably at least 85-90%, including about 91% or 95%.
- 15 In a related embodiment, the present invention provides a "sequencably pure" form of the amino acid sequence described herein. "Sequencably pure" is hereinbefore described as substantially homogeneous to facilitate amino acid determination.
- In a further related embodiment, the present invention provides a "substantially homogeneous" form of the subject amino acid sequence, wherein the term "substantially homogeneous" is hereinbefore defined as being in a form suitable for interaction with an immunologically interactive molecule. Preferably, the polypeptide is at least 20% homogeneous, more preferably at least 50% homogeneous, still more preferably at least 75% homogeneous and yet still more preferably at least about 95-100% homogeneous, in 25 terms of activity per microgram of total protein in the protein preparation.

The present invention further extends to a synthetic peptide of at least 5 amino acid residues in length derived from or comprising a part of the amino acid sequence set forth in any one or more of SEQ ID Nos:2, 6, 8, 10, 12 or 14, or having at least 40% similarity thereto.

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Those skilled in the art will be aware that such synthetic peptides may be useful in the production of immunologically interactive molecules for the preparation of antibodies or as the peptide component of an immunoassay.

5 The invention further extends to an antibody molecule such as a polyclonal or monoclonal antibody or an immunologically interactive part or fragment thereof which is capable of binding to a cellulose gene product according to any of the foregoing embodiments.

The term "antibody" as used herein, is intended to include fragments thereof which are also specifically reactive with a polypeptide of the invention. Antibodies can be fragmented using conventional techniques and the fragments screened for utility in the same manner as for whole antibodies. For example, F(ab')2 fragments can be generated by treating antibody with pepsin. The resulting F(ab')2 fragment can be treated to reduce disulfide bridges to produce Fab' fragments.

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Those skilled in the art will be aware of how to produce antibody molecules when provided with the cellulose gene product of the present invention. For example, by using a polypeptide of the present invention polyclonal antisera or monoclonal antibodies can be made using standard methods. A mammal, (e.g., a mouse, hamster, or rabbit) can be immunized with an immunogenic form of the polypeptide which elicits an antibody response in the mammal. Techniques for conferring immunogenicity on a polypeptide include conjugation to carriers or other techniques well known in the art. For example, the polypeptide can be administered in the presence of adjuvant. The progress of immunization can be monitored by detection of antibody titers in plasma or serum. Standard ELISA or other immunoassay can be used with the immunogen as antigen to assess the levels of antibodies. Following immunization, antisera can be obtained and, if desired IgG molecules corresponding to the polyclonal antibodies may be isolated from the sera.

To produce monoclonal antibodies, antibody producing cells (lymphocytes) can be harvested 30 from an immunized animal and fused with myeloma cells by standard somatic cell fusion

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procedures thus immortalizing these cells and yielding hybridoma cells. Such techniques are well known in the art. For example, the hybridoma technique originally developed by Kohler and Milstein (1975) as well as other techniques such as the human B-cell hybridoma technique (Kozbor et al., 1983), the EBV-hybridoma technique to produce human monoclonal antibodies (Cole et al., 1985), and screening of combinatorial antibody libraries (Huse et al., 1989). Hybridoma cells can be screened immunochemically for production of antibodies which are specifically reactive with the polypeptide and monoclonal antibodies isolated.

As with all immunogenic compositions for eliciting antibodies, the immunogenically effective amounts of the polypeptides of the invention must be determined empirically. Factors to be considered include the immunogenicity of the native polypeptide, whether or not the polypeptide will be complexed with or covalently attached to an adjuvant or carrier protein or other carrier and route of administration for the composition, i.e. intravenous, intramuscular, subcutaneous, etc., and the number of immunizing doses to be administered. Such factors are known in the vaccine art and it is well within the skill of immunologists to make such determinations without undue experimentation.

It is within the scope of this invention to include any second antibodies (monoclonal, polyclonal or fragments of antibodies) directed to the first mentioned antibodies discussed above. Both the first and second antibodies may be used in detection assays or a first antibody may be used with a commercially available anti-immunoglobulin antibody.

The present invention is further described by reference to the following non-limiting Figures and Examples.

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In the Figures:

Figure 1 is a photographic representation showing the inflorescence length of wild-type Arabidopsis thaliana Columbia plants (plants 1 and 3) and rsw1 plants (plants 2 and 4) grown at 21°C (plants 1 and 2) or 31°C. Plants were grown initially at 21°C until bolting commenced, the bolts were removed and the re-growth followed in plants grown at each temperature.

Figure 2 is a photographic representation of a cryo-scanning electron micrograph showing misshapen epidermal cells in the cotyledons and hypocotyl of the *rsw*1 mutant when grown at 31°C for 10 days.

Figure 3 is a graphical representation of a gas chromatograph of alditol acetates of methylated sugars from a cellulose standard (top panel) and from the neutral glucan derived from shoots of rsw1 plants grown at 31°C (lower panel). The co-incident peaks show that the rsw1 glucan is 1,4-linked.

Figure 4 is a schematic representation of the contiguous region of Arabidopsis thaliana chromosome 4 (stippled box) between the cosmid markers g8300 and 06455, showing the location of overlapping YAC clones (open boxes) within the contiguous region. The position of the RSW1 locus is also indicated, approximately 1.2cM from g8300 and 0.9cM from 06455. The scale indicates 100kb in length. L, left-end of YAC; R, right-end of YAC. Above the representation of chromosome 4, the YAC fragments and cosmid clone fragments used to construct the contiguous region are indicated, using a prefix designation 25 corresponding to the YAC or cosmid from which the fragments were obtained (eg yUP9E3, yUP20B12, etc) and a suffix designation indicating whether the fragment corresponds to the right-end (RE) or left-end (LE) of the YAC clone; N, North; S, South; CAPS, cleaved amplified polymorphic sequence (Konieczny and Ausubel, 1993) version of the g8300 marker.

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Figure 5 is a schematic representation of a restriction map of construct 23H12 between the left T-DNA border (LB) and right T-DNA border (RB) sequences (top solid line), showing the position of the Arabidopsis thaliana RSW1 locus (stippled box). The line at the top of the figure indicates the region of 23H12 which is contained in construct pRSW1. The structure of the RSW1 gene between the translation start (ATG) and translation stop (TAG) codons is indicated at the bottom of the figure. Exons are indicated by filled boxes; introns are indicated by the solid black line. The alignment of EST clone T20782 to the 3'-end of the RSW1 gene, from near the end of exon 7 to the end of exon 14, is also indicated at the bottom of the figure. Restriction sites within 23H12 are as follows: B, BamHI; E, EcoRI; 10 H, HindIII; S, SalI; Sm. SmaI.

Figure 6 is a photographic representation showing complementation of the radial root swelling phenotype of the rsw1 mutant by transformation with construct 23H12. The rsw1 mutant was transformed with 23H12 as described in Example 6. Transformed rsw1 plants (centre group of three seedlings), untransformed rsw1 plants (left group of three seedlings) and untransformed A.thaliana Columbia plants (right group of three seedlings) were grown at 21°C for 5 days and then transferred to 31°C for a further 2 days, after which time the degree of root elongation and radial root swelling was determined.

- 20 Figure 7 is a photographic representation comparing wild-type Arabidopsis thaliana Columbia plants (right-hand side of the ruler) and A.thaliana Columbia plants transformed with the antisense RSW1 construct (i.e. EST T20782 expressed in the antisense orientation under control of the CaMV 35S promoter sequence; left-hand side of the ruler), showing inflorescence shortening at 21°C in plants transformed with the antisense RSW1 construct compared to untransformed Columbia plants. The phenotype of the antisense plants at 21°C is similar to the phenotype of the rsw1 mutant at 31°C. Inflorescence height is indicated in millimetres.
- Figure 8 is a schematic representation showing the first 90 amino acid residues of 30 Arabidopsis thaliana RSW1 aligned to the amino acid sequences of homologous polypeptides

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from A. thaliana and other plant species. The shaded region indicates highly conserved sequences. Ath-A and Ath-B are closely related Arabidopsis thaliana cDNA clones identified by hybridisation screening using part of the RSW1 cDNA as a probe. S0542, rice EST clone (MAFF DNA bank, Japan); celA1 and celA2, cotton cDNA sequences expressed in cotton fibre (Pear et al, 1996); SOYSTF1A and SOYSTF1B, putative soybean bZIP transcription factors. Amino acid designations are as indicated in Table 1 incorporated herein. Conserved cysteine residues are indicated by the asterisk.

Figure 9 is a schematic representation showing the alignment of the complete amino acid sequence of Arabidopsis thaliana RSW1 to the amino acid sequences of homologous polypeptides from A. thaliana and other plant species. The shaded region indicates highly conserved sequences. Ath-A and Ath-B are closely related Arabidopsis thaliana cDNA clones identified by hybridisation screening using part of the RSW1 cDNA as a probe. S0542, rice EST clone (MAFF DNA bank, Japan); celA1, cotton genetic sequence (Pear et al, 1996); D48636, a partial cDNA clone obtained from rice (Pear et al, 1996). Amino acid designations are as indicated in Table 1 incorporated herein. Numbering indicates the amino acid position in the RSW1 sequence.

Figure 10 is a schematic representation of the RSW1 polypeptide, showing the positions of putative transmembrane helices (hatched boxes), cysteine-rich region (Cys) and aspartate residues (D) and the QVLRW signature which are conserved between RSW1 and related amino acid sequences. Regions of RSW1 which are highly-conserved between putative cellulose biosynthesis polypeptides are indicated by the dark-shaded boxes, while less-conserved regions are indicated by the light-shaded boxes.

25

Figure 11 is a photographic representation of a Southern blot hybridisation of the 5'- end of the *Arabidopsis thaliana* RSW1 cDNA to *BgI*II-digested DNA derived from *A. thaliana* (lane 1) and cotton (lane 2). Hybridisations were carried out under low stringency conditions at 55°C. Arrows indicate the positions of hybridising bands.

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EXAMPLE 1

CHARACTERISATION OF THE CELLULOSE-DEFICIENT

Arabidopsis thaliana MUTANT rsw1

5 1. Morphology

The Arabidopsis thaliana rsw1 mutant was produced in a genetic background comprising the ecotype Columbia.

The altered root cell-shape and temperature sensitivity of the root morphology of the 10 Arabidopsis thaliana mutant rsw1 are disclosed, among other morphological mutants, by Baskin et al. (1992).

As shown in Figure 1, the present inventors have shown that the rsw1 mutant exhibits the surprising phenotype of having reduced inflorescence height when grown at 31°C, compared to wild-type Columbia plants grown under similar conditions. In contrast, when grown at 21°C, the inflorescence height of rsw1 is not significantly different from wild type plants grown under similar conditions, indicating that the shoot phenotype of rsw1 is conditional and temperature-dependent.

- 20 Furthermore, cryo-scanning electron microscopy of the epidermal cells of the *rsw1* mutant indicates significant abnormality in cell shape, particularly in respect of those epidermal cells forming the leaves, hypocotyl and cotyledons, when the seedlings are grown at 31°C (Figure 2).
- 25 Rosettes (terminal complexes) are the putative hexameric cellulose synthase complexes of higher plant plasma membranes (Herth, 1985). Freeze-fractured root cells of Arabidopsis thaliana rsw1 plants grown at 18°C show cellulose microfibrils and rosettes on the PF face of the plasma membrane that resembles those of wild-type A. thaliana and other angiosperms. Transferring the rsw1 mutant to 31°C reduces the number of rosettes in the 30 mutant within 30 min, leading to extensive loss after 3 hours. Plasma membrane particles

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align in rows on prolonged exposure to the restrictive temperature. In contrast, there is no change in the appearance of cortical microtubules that align cellulose microfibrils, or of Golgi bodies that synthesise other wall polysaccharides and assemble rosettes.

5 2. Carbohydrate content

The effect of mutations in the RSWI gene on the synthesis of cellulose and other carbohydrates was assessed by measuring in vivo incorporation of ¹⁴C (supplied as uniformly labelled glucose) into various cell wall fractions. Wild type (RSW1) and homozygous mutant rsw] seed were germinated at 21°C on agar containing Hoagland's nutrients and 1% (w/v) 10 unlabelled glucose. After 5 d, half of the seedlings were transferred to 31°C for 1 d while the remainder were maintained at 21 °C for the same time. Seedlings were covered with a solution containing Hoagland's nutrients and ¹⁴C-glucose and incubated for a further 3 h at the same temperature. Rinsed roots and shoots were separated and frozen in liquid nitrogen. Tissue was homogenised in cold, 0.5 M potassium phosphate buffer (0.5M KH₂PO₄, pH7.0) 15 and a crude cell wall fraction collected by centrifugation at 2800 rpm. The wall fraction was extracted with chloroform/methanol [1:1 (v/v)] at 40°C for 1 hour, followed by a brief incubation at 150°C, to remove lipids. The pellet was washed successively with 2ml methanol, 2ml acetone and twice with 2ml of deionised water. Finally, the pellet was extracted successively with dimethyl sulphoxide under nitrogen to remove starch: 0.5% 20 ammonium oxalate to remove pectins; 0.1 M KOH and 3 mg/ml NaBH4 and then with 4 M KOH and 3 mg/ml NaBH₄ to extract hemicelluloses; boiling acetic acid/nitric acid/water [8:1:2 (v/v)], to extract any residual non-cellulosic carbohydrates and leave crystalline cellulose as the final insoluble pellet (Updegraph, 1969). All fractions were analysed by liquid scintillation counting and the counts in each fraction from the mutant were expressed 25 as a percentage of the counts in the wild type under the same conditions.

As shown in Table 3, mutant and wild type plants behave in quite similar fashion at 21°C (the permissive temperature) whereas, at the restrictive temperature of 31°C, the incorporation of ¹⁴C into cellulose is severely inhibited (to 36% of wild type) by the *rsw*1 30 mutation. The data in Table 3 indicate that cellulose synthesis is specifically inhibited in

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the rsw1 mutant. The wild type RSW1 gene is therefore involved quite directly in cellulose synthesis and changing its sequence by mutation changes the rate of synthesis.

5 TABLE 3

| Counts in fractions from rsw1 plants expressed as a % of counts in comparable fraction from wild type plants | | | | | |
|--|------|----------------|------|-----------|------|
| Pectins | | Hemicelluloses | | Cellulose | |
| 21°C | 31°C | 21°C | 31°C | 21°C | 31°C |
| 125 | 104 | 111 | 101 | 80 | 36 |

10

In homozygous mutant rsw1 plants, the pectin fraction extracted by ammonium oxalate contained abundant glucose, atypical of true uronic acid-rich pectins. The great majority of the glucose remained in the supernatant when cetyltrimethylammonium bromide precipitated 15 the negatively charged pectins.

3. Non-crystalline β-1,4-glucan content

The quantity of cellulose and the quantity of a non-crystalline β-1,4-glucan recovered from the ammonium oxalate fraction were determined for seedlings of wild type Columbia and for 20 backcrossed, homozygous rswl that were grown for either 7 days at 21°C or alternatively, for 2 days at 21°C and 5 days at 31°C, on vertical agar plates containing growth medium (Baskin et al., 1992) plus 1% (w/v) glucose, and under continuous light (90 μmol m⁻² s⁻¹). Roots and shoots were separated from about 150 seedlings, freeze-dried to constant weight and ground in a mortar and pestle with 3 ml of cold 0.5 M potassium phosphate buffer (pH 7.0). The combined homogenate after two buffer rinses (2ml each) was centrifuged at 2800 x g for 10 min. After washing the pellet fraction twice with 2 ml buffer and twice with 2 ml distilled water, the pellet, comprising the crude cell wall fraction, and the pooled supernatants, comprising the phosphate buffer fraction were retained. The crude cell wall pellet fraction was stirred with two 3 ml aliquots of chloroform/methanol [1:1 (v/v)] for 1 hour at 40°C, 2 ml of methanol at 40°C for 30 min, 2 ml of acetone for 30 min, and twice with water. The whole

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procedure repeated in the case of shoots. Combined supernatants were dried in a nitrogen stream. The pellet was successively extracted with: (i)3 ml of DMSO- water 9:1 [v/v], sealed under nitrogen, overnight with shaking, followed by two 2ml extractions using DMSO/water and three 2ml water washes; (ii) 3ml of ammonium oxalate (0.5 %) at 100°C for 1 hour, followed by two water washes; (iii) 3ml of 0.1 M KOH containing 1mg/ ml sodium borohydride, for 1 hour at 25°C (repeated once for root material or twice for shoot material), with a final wash with 2 ml water; (iv) 3 ml of 4 M KOH containing 1 mg/ml sodium borohydride, for 1 hour at 25°C (repeated once for root material or twice for shoot material). The final pellet was boiled with intermittent stirring in 3 ml of acetic acid-nitric acid-water [8:1:2 (v/v)] (Updegraph 1969), combined with 2 water washes, and diluted with 5 ml water.

The insoluble residue of cellulose was solubilised in 67% (v/v) H₂SO₄, shown to contain greater than 97% (w/v) glucose using GC/MS (Fisons AS800/MD800) of alditol acetates (Doares *et al.*, 1991) and quantified in three independent samples by anthrone/H₂SO₄ reaction.

15 Results of GC/MS for pooled replica samples are presented in Table 4.

The non-crystalline β-1,4-glucan was recovered as the supernatant from the ammonium oxalate fraction when anionic pectins were precipitated by overnight incubation at 37 °C with 2% (w/v) cetyltrimethylammonium bromide (CTAB) and collected by centrifugation at 2800 x g for 10 min. The glucan (250 µg/ml) or starch (Sigma; 200 µg/ml) were digested with mixtures of endocellulase (EC 3.2.1.4; Megazyme, Australia) from *Trichoderma* and almond β-glucosidase (EC 3.2.1.21; Sigma), or *Bacillus sp.* α-amylase (EC 3.2.1.1; Sigma) and rice α-glucosidase (EC 3.2.1.20; Sigma).

- 25 The material recovered in the supernatant from the ammonium oxalate fraction was shown to contain a pure β-1,4-glucan by demonstrating that: (i) only glucose was detectable when it was hydrolysed by 2 M TFA in a sealed tube for 1 h at 120°C in an autoclave, the supernatant (2000 g for 5 min) was dried under vacuum at 45°C to remove TFA and glucose was determined by GC/MS;
 (ii) methylation (Needs and
- 30 Selvendran 1993) gave a dominant peak resolved by thin layer chromatography and by GC/MS

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that was identical to that from a cellulose standard and so indicative of 1,4-linked glucan (Figure 3); and

(iii) the endo-cellulase and β-1,4-glucosidase mixture released 83 % of the TFA-releasable glucose from the glucan produced by rswl at 31°C while 5 the α-amylase/α-glucosidase mixture released no glucose from the glucan. Conversely, the α-amylase/α-glucosidase mixture released 95% of the TFA-releasable glucose from a starch sample, while the endo-cellulase/β-1,4-glucosidase mixture released no glucose from starch.

Extractability of the glucan using ammonium oxalate, and the susceptibility of the glucan to endocellulase/β-glucosidase and TFA hydrolysis indicate that the glucan in the rswl mutant is not crystalline, because it is the crystallinity of glucan which makes cellulose resistant to extraction and degradation.

Table 4 shows the quantity of glucose in cellulose determined by the anthrone/H₂SO₄ reaction and the quantity in the non-crystalline glucan after TFA hydrolysis, for shoots of wild type and mutant rsw1 Arabidopsis plants. The data indicate that the production of cellulose and of the non-crystalline β-1,4-glucan can be manipulated by mutational changes in the RSW1 gene.

TABLE 4

20 Glucose contents of cellulose and of the ammonium oxalate-extractable glucan

| | wild type | | rswl | |
|-----------|-----------|---------|--------|---------|
| | 21°C | 31°C | 21°C | 31°C |
| Cellulose | 273+28 | 363+18* | 218+20 | 159+19* |
| Glucan | 22 | 58 | 24 | 195 |

All values nmol glucose mg-1 plant dry weight + sd (n=3).

25 * Differences significant at 0.001 % level.

4. Starch content

The quantity of starch recovered in the DMSO fraction from roots in the experiment described above was also determined by the anthrone/H₂SO₄ extraction (Table 5).

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As shown in Table 5, the level of starch deposited in the rsw1 mutant is 4-fold that detectable in the roots of wild-type plants at the restrictive temperature of 31°C. A similar rise in starch is also seen if the data are expressed as nmol glucose per plant. There is no detectable difference in deposition at starch between rsw1 plants and wild-type plants at 5 21°C.

TABLE 5

Quantity of starch (nmol glucose per mg dry weight of seedling) extracted from roots of rsw1 and wild type seedlings

| | | Phenotype | | |
|----|-------------|-----------|-------------|--|
| 10 | Temperature | Wild-type | rsw1 mutant | |
| | 21°C | 22 | 18 | |
| | 31°C | 37 | 126 | |

The composition of cell walls in the rsw1 mutant plant compared to wild type plants at the 15 restrictive temperature of 31°C, is summarised in Table 6.

TABLE 6

Mol% composition of cell walls from shoots of rsw1 and wild-type seedlings grown at 31°C

| | Phenotype | | |
|----------------------------------|-----------|-------------|--|
| Cell wall component | Wild-type | rsw1 mutant | |
| Crystalline cellulose | 38.4 | 16.5 | |
| Non- crystalline β-1,4-glucan | 8.5 | 27.1 | |
| Pectin | 37.1 | 36.3 | |
| Alkali-soluble | 15.6 | 19.8 | |
| Acid-soluble | 0.3 | 0.4 | |

25

20

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In conclusion, the *rsw*1 mutation disassembles cellulose synthase complexes in the plasma membrane, reduces cellulose accumulation and causes β -1,4-glucan to accumulate in a non-crystalline form.

5

EXAMPLE 2 MAPPING OF YAC CLONES TO THE rsw1 LOCUS

The rsw1 locus in the mutant Arabidopsis thaliana plant described in Example 1 above was 10 mapped to chromosome 4 of A. thaliana using RFLP gene mapping techniques(Chang et al., 1988; Nam et al., 1989) to analyse the F₂ or F₃ progeny derived from a Columbia (Co)/Landsberg (Ler) cross. In particular, the rsw1 mutation was shown to be linked genetically to the ga5 locus, which is a chromosome 4 visual marker in A. thaliana.

15 Based on an analysis of map distances and chromosomal break points in 293 F₂ or F₃ progeny derived from a Columbia (Co)/Landsberg (Ler) cross, rswl was localised to an approximately 2.1 cM region between the RFLP markers g8300 and 06455, approximately 1.2cM south of the CAPS (cleaved amplified polymorphic sequence; Konieczny and Ausubel, 1993) version of the g8300 marker (Figure 4).

20

The interval between g8300 and 06455 in which rsw1 residues was found to be spanned by an overlapping set of Yeast Artificial Chromosome (YAC) clones. The clones were obtained from Plant Industry, Commonwealth Scientific and Industrial Research Organisation, Canberra, Australia. The YACs were positioned in the g8300/06455 interval by hybridisation using known DNA molecular markers (from within the interval) and DNA fragments from the ends of the YACs. The length of the interval was estimated to comprise 900kb of DNA.

Refined gene mapping of recombinants within the region spanned by YAC clones established 30 the genetic distance between the RFLP marker g8300 and the rsw1 locus.

- 50 -

The combination of genetic map distance data and the mapping of YAC clones within the region further localised the rswl locus to the YAC clone designated yUP5C8.

5 EXAMPLE 3

MAPPING OF cDNA CLONES TO THE YAC CLONE YUP5C8

An Arabidopsis thaliana cDNA clone designated T20782 was obtained from the public Arabidopsis Resource Centre, Ohio State University, 1735 Neil Avenue, Columbus, OH 43210, United States of America. The T20782 cDNA clone was localised broadly to the DNA interval on Arabidopsis chromosome 4 between the two markers g8300 and 06455 shown in Figure 4. Using a polymerase chain reaction (PCR) based approach DNA primers (5'-AGAACAGCAGATACACGGA-3' and 5'-CTGAAGAAGGCTGGACAAT-3') designed to the T20782 cDNA nucleotide sequence were used to screen Arabidopsis YAC clone libraries. The T20782 cDNA clone was found to localise to YACs (CIC1F9, CIC10E9, CIC11D9) identified on the Arabidopsis chromosome 4 g8300 and 06455 interval (Figure 4). The same approach was used to further localise clone T20782 to YAC clone yUP5C8, the same YAC designated to contain the rsw1 locus in the same chromosome interval (Figure 4).

20

Furthermore, amplification of the YAC clone yUP5C8 using primers derived from T20782 produces a 500bp fragment containing two putative exons identical to part of the T20782 nucleotide sequence, in addition to two intron sequences.

25 The cDNA T20782 was considered as a candidate gene involved in cellulose biosynthesis.

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EXAMPLE 4

NUCLEOTIDE SEQUENCE ANALYSIS OF THE CDNA CLONE T20782

5 The nucleotide sequence of the cDNA clone T20782 is presented in SEQ ID NO: 1. The nucleotide sequence was obtained using a Dye Terminator Cycle Sequencing kit (Perkin Elmer cat. #401384) as recommended by the manufacturer. Four template clones were used for nucleotide sequencing to generate the sequence listed. The first template was the cDNA clone T20782. This template was sequenced using the following sequencing primers:

10

- a)5'-CAATGCATTCATAGCTCCAGCCT-3'
- b)5'-AAAAGGCTGGAGCTATGAATGCAT-3'
- c)5'-TCACCGACAGATTCATCATACCCG-3'
- d)5'- GACATGGAATCACCTTAACTGCC-3'
- 15 e)5'-CCATTCAGTCTTGTCTTCGTAACC-3'
 - **1)5'-GGTTACGAAGACAAGACTGAAATGG-3'**
 - g)5'-GAACCTCATAGGCATTGTGGGCTGG-3'
 - h)5'-GCAGGCTCTATATGGGTATGATCC-3'
 - i)Standard M13 forward sequencing primer.
- j)Standard T7 sequencing primer.

The second template clone (T20782 SphI deletion clone) was constructed by creating a DNA deletion within the T20782 clone. The T20782 clone was digested with the restriction enzyme SphI, the enzyme was heat-killed, the DNA ligated and electroporated into NM522 E. coli host cells. The T20782 SphI deletion clone was then sequenced using a standard M13 forward sequencing primer. Two other deletion clones were made for DNA sequencing in a similar fashion but the restriction enzymes EcoRI and SmaI were used. The T20782 EcoRI deletion clone and the T20782 SmaI deletion clone were sequenced using a standard T7 sequencing primer. The DNA sequence shown in SEQ ID NO:1 is for one DNA strand only however those skilled in the art will be able to generate the nucleotide sequence of the

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complementary strand from the data provided.

The amino acid sequence encoded by clone T20782 was derived and is set forth in SEQ ID NO:2.

5

The T20782 clone encodes all but the first Aspartate (D) residue of the D, D, D, QXXRW signature conserved in the general architecture of β -glycosyl transferases. In particular, T20782 encodes 5 amino acid residues of the D, D, D, QXXRW signature, between amino acid positions 109 and 370 of SEQ ID NO:2. The conserved Aspartate, Aspartate,

- 10 Glutamine. Arginine and Tryptophan amino acid residues are shown below, in bold type, with the local amino acid residues also indicated:
 - 1. Amino acid residues 105 to 113 of SEQ ID NO:2:

LLNVDCDHY;

15 2. Amino acid residues 324 to 332 of SEQ ID NO:2:

SVTEDILTG; and

3. Amino acid residues 362 to 374 of SEQ ID NO:2:

DRLNOVLRWALGS.

- 20 It must be noted that these invariable amino acids merely indicate that the T20782 derived amino acid sequence belongs to a very broad group of glycosyl transferases. Some of these enzymes such as cellulose synthase, chitin synthase, alginate synthase and hyaluronic acid synthase produce functionally very different compounds.
- 25 The presence of the conserved amino acid residues merely indicate that the T20782 clone may encode a β-glycosyl transferase protein such as the cellulose gene product, cellulose synthase. The fact that the clone localises in the vicinity of a gene involved in cellulose biosynthesis is the key feature which now focus interest on the T20782 clone as a candidate for the RSW1 (cellulose synthase) gene.

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The T20782 potentially codes for a cellulose synthase.

EXAMPLE 5

5 NUCLEOTIDE SEQUENCE ANALYSIS OF THE GENOMIC CLONE 23H12

Clone 23H12 contains approximately 21kb of Arabidopsis thaliana genomic DNA in the region between the left border and right border T-DNA sequences, and localises to the RSW1 candidate YAC yUP5C8. Clone 23H12 was isolated by hybridisation using EST20782 insert DNA, from a genomic DNA library made for plant transformation. Cosmid 12C4 was also shown to hybridize to the cDNA clone T20782, however this cosmid appears to comprise a partial genomic sequence corresponding to the related Ath-A cDNA sequence set forth in SEQ ID NO:7, for which the corresponding amino acid sequence is set forth in SEQ ID NO:8.

15

A restriction enzyme map of clone 23H12 is presented in Figure 5.

Nucleotide sequence of 8411bp of genomic DNA in the binary cosmid clone 23H12 was obtained (SEQ ID NO:3) by primer walking along the 23H12 template, using a Dye 20 Terminator Cycle Sequencing kit (Perkin Elmer cat. #401384) as recommended by the manufacturer. The following primers at least, were used for DNA sequencing of the 23H12 clone DNA:

| | a)cs1-R | 5'-CAATGCATTCATAGCTCCAGCCT-3' |
|----|-----------|--------------------------------|
| 25 | b)cs1-F | 5'-AAAAGGCTGGAGCTATGAATGCAT-3' |
| | c)up | 5'-AGAACAGCAGATACACGGA-3' |
| | d)ve76-R2 | 5'-ATCCGTGTATCTGCTGTTCTTACC-3' |
| | e)est1-R | 5'-AATGCTCTTGTTGCCAAAGCAC-3' |
| | f)sve76-F | 5'-ATTGTCCAGCCTTCTTCAGG-3' |
| 30 | g)ve76-R | 5'-CTGAAGAAGGCTGGACAATGC-3' |

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| h)B12-R1 | 5'-AGGTAAGCATAGCTGAACCATC-3' |
|----------|--------------------------------|
| i)B12-R2 | 5'-AGTAGATTGCAGATGGTTTTCTAC-3' |
| j)B12-R3 | 5'-TTCAATGGGTCCACTGTACTAAC-3' |
| k)B12-R4 | 5'-ATTCAGATGCACCATTGTC-3' |
| | |

5

The structure of the RSW1 gene contained in cosmid clone 23H12 is also presented in Figure 5. As shown therein, coding sequences in 23H12, from the last 12 bp of exon 7 to the end of exon 14, correspond to the full T20782 cDNA sequence (i.e. SEQ ID NO:1). The nucleotide sequences of the RSW1 gene comprising exons 1 to 8 were amplified from 10 A.thaliana Columbia double-stranded cDNA, using amplification primers upstream of the RSW1 start site and a primer internal to the EST clone T20782.

The exons in the RSW1 gene range from 81bp to 585bp in length and all 5' and 3' intron/exon splice junctions conform to the conserved intron rule.

15

The RSW1 transcript comprises a 5'-untranslated sequence of at least 70bp in length, a 3243bp coding region and a 360bp 3'-untranslated region. Northern hybridization analyses indicate that the RSW1 transcript in wild-type A. thaliana roots, leaves and inflorescences is approximately 4.0kb in length, and that a similar transcript size occurs in mutant tissue 20 (data not shown).

The derived amino acid sequence of the RSW1 polypeptide encoded by the cosmid clone 23H12 (i.e. the polypeptide set forth in SEQ ID NO:6) is 1081 amino acids in length and contains the entire D, D, D, QXXRW signature characteristic of β-glycosyl transferase proteins, between amino acid position 395 and amino acid position 822. The conserved Aspartate, Glutamine, Arginine and Tryptophan residues are shown below, in bold type, with the local amino acid residues also indicated:

1. amino acid residues 391 to 399 of SEQ ID NO:6:

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2. Amino acid residues 557 to 565 of SEQ ID NO:6:

LLNVDCDHY;

3. Amino acid residues 776 to 784 of SEQ ID NO:6:

SVTEDILTG; and

4. Amino acid residues 814 to 826 of SEQ ID NO:6:

DRLNOVLRWALGS.

The second and third conserved Aspartate residues listed *supra*, and the fourth conserved amino acid sequence motif listed *supra* (i.e. QVLRW) are also present in the cDNA clone 10 T20782 (see Example 4 above).

The 23H12 clone potentially encodes a cellulose synthase.

15 EXAMPLE 6

COMPLEMENTATION OF THE rsw1 MUTATION

The complementation of the cellulose mutant plant rsw1 is the key test to demonstrate the function of the clone 23H12 gene product. Complementation of the rsw1 phenotype was demonstrated by transforming the binary cosmid clone 23H12, or a derivative clone thereof encoding a functional gene product, into the Arabidopsis thaliana cellulose mutant rsw1. Two DNA constructs (23H12 and pRSW1) were used to complement the rswl mutant plant line.

25 1. Construct 23H12

5

Clone 23H12 is described in Example 5 and Figure 5.

2. Construct pRSW1

The 23H12 construct has an insert of about 21kb in length. To demonstrate that any 30 complementation of the phenotype of the rsw1 mutation is the result of expression of the gene

which corresponds to SEQ ID NO:3, a genetic construct, designated as pRSW1, comprising the putative RSW1 gene with most of the surrounding DNA deleted, was produced. A restriction enzyme (RE) map of the RSW1 gene insert in pRSW1 is provided in Figure 5.

5 To produce pRSW1, the RSW1 gene was subcloned from cosmid 23H12 and cloned into the binary plasmid pBIN19. Briefly, Escherichia coli cells containing cosmid 23H12 were grown in LB medium supplemented with tetracyclin (3.5 mg/L). Plasmid DNA was prepared by alkaline lysis and digested sequentially with restriction enzymes PvuII and SalI. Two co-migrating fragments of 9 kb and 10 kb. respectively, were isolated as a single fraction from a 0.8% (w/v) agarose gel. The RSW1 gene was contained on the 10 kb PvuII/SalI fragment. The 9 kb fragment appeared to be a PvuII cleavage product not comprising the RSW1 gene. The restriction fragments were ligated into pBIN19 digested with Smal and Sall. An aliquot of the ligation mix was introduced by electroporation into E.coli strain XLB1. Colonies resistant to kanamycin (50 mg/L) were selected and subsequently characterised by restriction enzyme analysis to identify those clones which contained only the 10 kb PvuII/SalI fragment comprising the RSW1 gene, in pBIN19.

3. Transfer of the 23HI2 and pRSW1 constructs to Agrobacterium tumefaciens

Cosmid 23H12 was transferred to Agrobacterium by triparental mating, essentially as described by Ditta et al. (1980). Three bacterial strains as follows were mixed on solid LB medium without antibiotics: Strain 1 was an E. coli helper strain containing the mobilising plasmid pRK2013, grown to stationary phase; Strain 2 was E.coli containing cosmid 23H12, grown to stationary phase; and Strain 3 was an exponential-phase culture of A. tumefaciens strain AGL1 (Lazo et al., 1991). The mixture was allowed to grow over night at 28°C, before an aliquot was streaked out on solid LB medium containing antibiotics (ampicillin 50 mg/L, rifampicin 50 mg/L, tetracyclin 3.5 mg/L) to select for transformed A. tumefaciens AGL1. Resistant colonies appeared after 2-3 days at 28°C and were streaked out once again on selective medium for further purification. Selected colonies were then subcultured in liquid LB medium supplemented with rifampicin (50 mg/L) and tetracyclin (3.5 mg/L) and stored at -80°C.

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Plasmid pRSW1 (initially designated as p2029) was introduced into A. tumefaciens strain AGL1 by electroporation.

4. Transformation of rswl plants

5 The rswl plant line was transformed with constructs 23H12 and pRSW1 using vacuum infiltration essentially as described by Bechtold et al. (1993).

5. Analysis of radial swelling in transformants

Complementation of the radial swelling (rsw) phenotype, which is characteristic of the rsw1 mutant plant, was assayed by germinating transformed (i.e. T1 seed) rsw1 seeds obtained as described supra on Hoaglands plates containing 50µg/ml kanamycin. Plates containing the transformed seeds were incubated at 21°C for 10-12 days. Kanamycin-resistant seedlings were transferred to fresh Hoaglands plates containing 50µg/ml kanamycin and incubated at 31°C for 2 days. Following this incubation, the root tip was examined for a radial swelling phenotype. Under these conditions, the roots of wild-type plants do not show any radial swelling phenotype however, the roots of rsw1 plants show clear radial swelling at the root tip and also have a short root compared to the wild-type plants. As a consequence, determination of the radial swelling phenotype of the transformed plants was indicative of successful complementation of the rsw1 phenotype.

20

The kanamycin-resistant seedlings were maintained by further growth of seedlings at 21 °C, following the high temperature incubation. Once plants had recovered, the seedlings were transferred to soil and grown in cabinets at 21 °C (16 hr light/8 hr dark cycle). T2 seed was then harvested from mature individual plants.

25

Using the 23H12 construct for rswl transformation, a total of 262 kanamycin-resistant seedlings were obtained. All of these transformants were tested for complementation of the root radial swelling phenotype. A total of 230 seedlings showed a wild type root phenotype, while only 32 seedlings showed the radial swelling root phenotype characteristic of rswl plants. By way of example, Figure 6 shows the phenotypes of transformed seedlings compared

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to untransformed wild-type and rsw1 seedlings, following incubation at 31°C. As shown in Figure 6, there is clear complementation of the radial swelling phenotype in the transformed seedlings, with normal root length being exhibited by the transformed seedlings at 31°C

5 Using the pRSW1 construct for transformation, a total of 140 kanamycin-resistant seedlings were obtained. All of the 11 seedlings tested for complementation of the root radial swelling phenotype showed a wild type root phenotype and none of the seedlings showed any signs of radial swelling in the roots (data not shown).

10 6. General morphological analysis of the complemented rswl mutant line

Further characterisation of the complemented rswl plants has shown that other morphological characteristics of rswl have also been restored in the transgenic lines, for example the bolt (inflorescence) height, and the ability of the plants to grow wild type cotyledons, leaves, trichomes, siliques and flowers at 31°C (data not shown).

15

7. Biochemical complementation of the rswl mutant line

T2 seed from transformations using cosmid 23H12 as described *supra* or alternatively, using the binary plasmid pBin19 which lacks any *RSW*1 gene sequences, was sown on Hoagland's solid media containing kanamycin (50µg/ml), incubated for 2 days at 21°C and then transferred to 31°C for 5 days. Wild-type *A.thaliana* Columbia plants were grown under similar conditions but without kanamycin in the growth medium. Kanamycin resistant T2 seedlings which have at least one copy of the 23H12 cosmid sequence, and wild-type seedlings, were collected and frozen for cellulose analysis.

25 Cellulose levels were determined as acetic-nitric acid insoluble material (Updegraph, 1969) for 10 lines of kanamycin-resistant T2 plants transformed with the 23H12 cosmid sequence, and compared to the cellulose levels in rswl mutant plants, wild-type A.thaliana Columbia plants and A.thaliana Columbia plants transformed with the binary plasmid pBin19. The results are provided in Table 7.

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As shown in Table 7, the cellulose levels have been significantly elevated in the complemented rswl (T2) plants, compared to the cellulose levels measured in the rswl mutant parent plant. In fact, cellulose levels in the 23H12-transformed plants, expressed relative to the fresh weight of plant material or on a per seedling basis, are not significantly different from the cellulose levels of either wild-type Arabidopsis thaliana Columbia plants or A.thaliana Columbia transformed with the binary plasmid pBin19. These data indicate that the 23H12 cosmid is able to fully complement the cellulose-deficient phenotype of the rswl mutant.

Homozygous T3 lines are generated to confirm the data presented in Table 7.

10

Furthermore, data presented in Table 7 indicate that there is no difference in the rate of growth of the T2 transformed rsw1 plants and wild-type plants at 31°C, because the fresh weight of such plants does not differ significantly. In contrast, the fresh weight of mutant rsw1 seedlings grown under identical conditions is only approximately 55% of the level observed in T2 lines transformed with 23H12 (range about 30% to about 80%). These data support the conclusion that cellulose levels have been manipulated in the complemented rsw1 (T2) plants.

Furthermore, the rate of cellulose synthesis in 23H12-transformed plants and wild-type 20 plants at 31°C, as measured by ¹⁴C incorporation is also determined.

Furthermore, the β -1,4-glucan levels and starch levels in the 23H12 transformant lines are shown to be similar to the β -1,4-glucan and starch levels in wild-type plants.

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TABLE 7
CELLULOSE LEVELS IN rsw1 PLANTS TRANSFORMED
WITH COSMID CLONE 23H12

5

| | PLANT LINE | SAMPLE SIZE (No. of plants) | SEEDLING FRESH WEIGHT (mg) | CELLULOSE (mg cellulose/ 100 mg tissue) | CELLULOSE (mg cellulose/ seedling) |
|----|----------------------|-----------------------------|----------------------------|---|------------------------------------|
| | 1.2 (rsw1+23H12) | 126 | 2.51 | 1.23 | 0.031 |
| 10 | 1.4 (rsw1+23H12) | 132 | 2.25 | 2.50 | 0.056 |
| | 2.1 (rsw1+23H12) | 126 | 3.23 | 1.29 | 0.042 |
| | 3.1 (rsw1+23H12) | 127 | 3.75 | 1.23 | 0.046 |
| | 3.10 (rsw1+23H12) | 128 | 3.52 | 1.69 | 0.060 |
| 15 | 4.4 (rsw1+23H12) | 110 | 5.14 | 1.31 | 0.067 |
| | 4.5 (rsw1+23H12) | 125 | 3.18 | 1.26 | 0.040 |
| | 5.3 (rsw1+23H12) | 124 | 2.77 | 1.17 | 0.032 |
| | 9.2 (rsw1+23H12) | 125 | 2.26 | 1.41 | 0.032 |
| 20 | 10.8 (rsw1+23H12) | 126 | 2.4 | 1.20 | 0.029 |
| | Columbia/pBin19 | 106 | 2.64 | 1.34 | 0.035 |
| | Columbia | 178 | 2.73 | 1.18 | 0.032 |
| | rswl mutant | 179 | 1.77 | 0.84 | 0.015 |

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EXAMPLE 7

DETERMINATION OF THE FULL-LENGTH NUCLEOTIDE SEQUENCE ENCODING THE WILD-TYPE RSW1 POLYPEPTIDE

5 Arabidopsis thaliana double-stranded cDNA and cDNA libraries were prepared using the CAPFINDER cDNA kit (Clontech). RNA was isolated from wild-type Columbia grown in sterile conditions for 21 days.

Approximately 100,000 cDNA clones in an unamplified cDNA library were screened under standard hybridization conditions at 65°C, using a probe comprising ³²P-labelled DNA amplified from double stranded cDNA. To prepare the hybridization probe, the following amplification primers were used:

- 1. 2280-F:5'GAATCGGCTACGAATTTCCCA 3'
- 2. 2370-F:5'TTGGTTGCTGGATCCTACCGG 3'
- 15 3. csp1-R:5'GGT TCT AAA TCT TCC GTC 3'

wherein the primer combinations were either 2280-F/csp1-R or 2370-F/csp1-R. The primer 2280-F corresponds to nucleotide positions 2226 to 2246 in SEQ ID NO:3, upstream of the translation start site. The primer 2370-F corresponds to nucleotide positions 2314 to 2334 in SEQ ID NO:3, encoding amino acids 7 through 13 of the RSW1 polypeptide. The primer csp1-R comprises nucleotide sequences complementary to nucleotides 588 to 608 of the T20782 clone (SEQ ID NO:1) corresponding to nucleotides 6120 to 6140 of SEQ ID NO:3. The hybridization probes produced are approximately 1858 nucleotides in length (2280-F/csp1-R primer combination) or 1946 nucleotides in length (2370-F/csp1-R primer 25 combination).

Five hybridizing bacteriophage clones were identified, which were plaque-purified to homogeneity during two successive rounds of screening. Plasmids were rescued from the positively-hybridizing bacteriophage clones, using the Stratagene excision protocol for the 30 ZapExpressTM vector according to the manufacturer's instructions. Colony hybridizations

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confirmed the identity of the clones.

Isolated cDNA clones were sequenced by primer walking similar to the method described in Examples 4 and 5 supra.

5

A full-length wild-type RSW1 nucleotide sequence was compiled from the nucleotide sequences of two cDNA clones. First, the 3'-end of the cDNA, encoding amino acids 453-1081 of RSW1, corresponded to the nucleotide sequence of the EST clone T20782 (SEQ ID NO:1). The remaining cDNA sequence, encoding amino acids 1-654 of RSW1, was 10 generated by amplification of the 5'-end from cDNA, using primer 2280-F, which comprises nucleotide sequences approximately 50-70bp upstream of the RSW1 translation start site in cosmid 23 H12, and primer csp1-R, which comprises nucleotide sequences complementary to nucleotides 588 to 608 of the T20782 clone (SEQ ID NO:1).

- 15 Several amplified clones are sequenced to show that no nucleotide errors were introduced by the amplification process. The 5' and 3' nucleotide sequences are spliced together to produce the complete RSW1 open reading frame and 3'-untranslated region provided in SEQ ID NO:5.
- 20 Those skilled in the art will be aware that the 5'-end and 3'-end of the two incomplete cDNAs are spliced together to obtain a full-length cDNA clone, the nucleotide sequence of which is set forth in SEQ ID NO:5.

Of the remaining cDNA clones, no isolated cDNA clone comprised a nucleotide sequence 25 which precisely matched the nucleotide sequence of the RSW1 gene present in cosmid 23H12. However, several clones containing closely-related sequences were obtained, as summarised in Table 8. The nucleotide sequences of the Ath-A and Ath-B cDNAs are provided herein as SEO ID Nos: 7 and 9, respectively.

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TABLE 8
CHARACTERISATION OF A. thaliana cDNA CLONES

| | CLONE NAME | DESCRIPTION | LENGTH | SEQ ID NO: |
|---|------------|--------------------|-------------|--------------|
| | RSW1.1A | chimeric clone | partial | not provided |
| 5 | RSW1A | chimeric clone | partial | not provided |
| | Ath-A | 12C4 cDNA | full-length | SEQ ID NO:7 |
| Ī | Ath-B | new sequence | full-length | SEQ ID NO:9 |
| Ī | RSW4A | identical to Ath-B | full-length | not provided |

10 The derived amino acid sequences encoded by the cDNAs listed in Table 8, is provided in Figures 8 and 9 and SEQ ID Nos: 8 and 10 herein.

Figure 10 a schematic representation of the important features of the RSW1 polypeptide which are conserved within A.thaliana and between A.thaliana and other plant species. In addition to the species indicated in Figure 10, the present inventors have also identified maize, wheat, barley and Brassica ssp. cellulose biosynthetic genes by homology search. Accordingly, the present invention extends to cellulose genes and cellulose biosynthetic polypeptides as hereinbefore defined, derived from any plant species, including A. thaliana, cotton, rice, wheat, barley, maize, Eucalyptus ssp., Brassica ssp. Pinus ssp., Populus ssp., 20 Picea ssp., hemp, jute and flax, amongst others.

EXAMPLE 8 ISOLATION OF FULL-LENGTH NUCLEOTIDE SEQUENCE ENCODING THE MUTANT RSW1 POLYPEPTIDE

25

Arabidopsis thaliana double-stranded cDNA and cDNA libraries were prepared using the CAPFINDER cDNA kit (Clontech). RNA was isolated from Arabidopsis thaliana Columbia rsw1 mutant plants grown in sterile conditions for 21 days.

30 The full-length rsw1 mutant nucleotide sequence was generated by sequencing two amplified

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DNA fragments spanning the *rsw1* mutant gene. The 5'- end sequence of the cDNA (comprising the 5'-untranslated region and exons 1-11) was amplified using the primer combination 2280-F/csp1-R (Example 7). The 3'-end sequence was amplified using the primers EST1-F and cs3-R set forth below:

1.Primer EST1-F:

5

25

5'AATGCTTCTTGTTGCCAAAGCA 3'

2.Primer cs3-R:

5'GACATGGAATCACCTTAACTGCC 3'

wherein primer EST1-F corresponds to nucleotide positions 1399-1420 of SEQ ID NO:5 (within exon 8) and primer cs3-R is complementary to nucleotides 3335-3359 of SEQ ID NO:5 (within the 3'-untranslated region of the wild-type transcript).

The full-length sequence of the mutant rsw1 transcript is set forth herein as SEQ ID NO:11.

Whilst not being bound by any theory or mode of action, a single nucleotide substitution in the rsw1 mutant nucleotide sequence (nucleotide position 1716 in SEQ ID NO:11), relative to the wild-type RSW1 nucleotide sequence (nucleotide position 1646 in SEQ ID NO:5), resulting in Ala549 being substituted with Val549 in the mutant polypeptide, may contribute to the altered activity of the RSW1 polypeptide at non-permissive temperatures such as 31°C. Additional amino acid substitutions are also contemplated by the present invention, to alter the activity of the RSW1 polypeptide, or to make the polypeptide temperature-sensitive.

EXAMPLE 9 ANTISENSE INHIBITION OF CELLULOSE PRODUCTION

IN TRANSGENIC PLANTS

1. Construction of an antisense RSW1 binary vector

One example of transgenic plants in which cellulose production is inhibited is provided by the expression of an antisense genetic construct therein. Antisense technology is used to 30 target expression of a cellulose gene(s) to reduce the amount of cellulose produced by

transgenic plants.

By way of exemplification, an antisense plant transformation construct has been engineered to contain the T20782 cDNA insert (or a part thereof) in the antisense orientation and in operable connection with the CaMV 35S promoter present in the binary plasmid pRD410 (Datla et al. 1992). More particularly, the T20782 cDNA clone, which comprises the 3'-end of the wild-type RSW1 gene, was digested with XbaI and KpnI and cloned into the kanamycin-resistant derivative of pGEM3zf(-), designated as plasmid, pJKKMf(-). The RSW1 sequence was sub-cloned, in the antisense orientation, into the binary vector pRD410 as a XbaI/SacI fragment, thereby replacing the β-glucuronidase (GUS or uidA) gene. This allows the RSW1 sequence to be transcribed in the antisense orientation under the control of the CaMV 35S promoter.

The antisense RSW1 binary plasmid vector was transferred to Agrobacterium tumefaciens strain AGL1, by triparental mating and selection on rifampicin and kanamycin, as described by Lazo et al. (1991). The presence of the RSW1 insert in transformed A.tumefaciens cells was confirmed by Southern hybridization analysis (Southern, 1975). The construct was shown to be free of deletion or rearrangements prior to transformation of plant tissues, by back-transformation into Escherichia coli strain JM101 and restriction digestion analysis.

20

2. Transformation of Arabidopsis thaliana

Eight pots, each containing approximately 16 A. thaliana ecotype Columbia plants, were grown under standard conditions. Plant tissue was transformed with the antisense RSW1 binary plasmid by vacuum infiltration as described by Bechtold et al (1993). Infiltration media contained 2.5% (w/v) sucrose and plants were infiltrated for 2 min until a vacuum of approximately 400mm Hg was obtained. The vacuum connection was shut off and plants allowed to sit under vacuum for 5 min.

Approximately 34,000 T1 seed was screened on MS plates containing 50µg/ml kanamycin, 30 to select for plants containing the antisense RSW1 construct. Of the T1 seed sown, 135

kanamycin-resistant seedlings were identified, of which 91 were transferred into soil and grown at 21°C under a long-day photoperiod (16hr light; 8hr dark).

Of the 91 transgenic lines, 19 lines were chosen for further analysis which had anther 5 filaments in each flower which were too short to deposit pollen upon the stigma and, as a consequence, required hand-pollination to obtain T2 seed therefrom.

T2 seed from 14 of these 19 lines was plated out onto vertical Hoaglands plates containing kanamycin to determine segregation ratios. Between five and ten seed were plated per transgenic line. Control seeds, including A. thaliana Columbia containing the binary vector pBIN19 (Bevan, 1984) and segregating 3:1 for kanamycin resistance, and the rswl mutant transformed with the NPTII gene, also segregating 3:1 for kanamycin resistance, were grown under the same conditions. Kanamycin-resistant plants were transferred to soil and grown at 21°C under long days, until flowering. Untransformed Arabidopsis thaliana Columbia plants were also grown under similar conditions, in the absence of kanamycin.

3. Morphology of antisense- RSW1 plants

A comparison of the morphology of antisense RSW1 plants grown at 21°C, to mutant rswl plants grown at the non-permissive temperature (i.e. 31°C) has identified a number of common 20 phenotypes. For example, the antisense plants exhibit reduced fertility, inflorescence shortening and have short anthers, compared to wild-type plants, when grown at 21°C. These phenotypes are also observed in mutant rswl plants grown at 31°C. These results suggest that the antisense construct in the transgenic plants may be targeting the expression of the wild-type RSW1 gene at 21°C.

25

Figure 7 shows the reduced inflorescence (bolt) height in antisense 35S-RSW1 plants compared to wild-type A. thaliana Columbia plants grown under identical conditions.

4. Cell wall carbohydrate analysis of antisense plants.

30 T3 plants which are homozygous for the 35S-RSW1 antisense construct are generated and the

content of cellulose therein is determined as described in Example 1. Plants expressing the antisense construct are shown to have significantly less cellulose in their cell walls, compared to wild-type plants. Additionally, the levels of non-crystalline β-1,4-glucan and starch are elevated in the cells of antisense plants, compared to otherwise isogenic plant lines which have not been transformed with the antisense genetic construct.

5. Antisense 35S-RSW1 mRNA expression levels in transgenic plants

Total RNA was extracted from 0.2g of leaf tissue derived from 33 kanamycin-resistant T1 plants containing the antisense 35S-RSW1 genetic construct, essentially according to 10 Longemann et al. (1986). Total RNA (25 μg) was separated on a 2.2M formaldehyde/agarose gel, blotted onto nylon filters and hybridized to a riboprobe comprising the sense strand sequence of the cDNA clone T20782. To produce the riboprobe, T7 RNA polymerase was used to transcribe sense RNA from a linearised plasmid template containing T20782, in the presence of [α-12P]UTP. Hybridizations and subsequent washes were performed as described by Dolferus et al. (1994). Hybridized membranes were exposed to Phosphor screens (Molecular Dynamics, USA).

The levels of expression of the RSW1 antisense transcript were determined and compared to the level of fertility observed for the plant lines. As shown in Table 9, the level of antisense gene expression is correlated with the reduced fertility phenotype of the antisense plants. In 13 lines, a very high or high level of expression of the 35S-RSW1 antisense gene was observed and, in 11 of these lines fertility was reduced. Only lines 2W and 3E which expressed high to very high levels of antisense mRNA, appeared to be fully fertile. In 12 lines which expressed medium levels of antisense mRNA, approximately one-half were fertile and one-half appeared to exhibit reduced fertility. In contrast, in 8 plant lines in which only a low or very low level of expression of the antisense 35S-RSW1 genetic construct was observed, a wild-type (i.e. fertile) phenotype was observed for all but one transgenic line, line 2R.

Data presented in Table 9 and Figure 7 indicate that the phenotype of the cellulose-deficient 30 mutant rswl may be reproduced by expressing antisense RSW1 genetic constructs in transgenic

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plants.

To confirm reduced cellulose synthesis and/or deposition in transgenic plants expressing the antisense RSW1 gene, the level of cellulose is measured by the ¹⁴C incorporation assay or as acetic/nitric acid insoluble material as described in Example 1 and compared to cellulose production in otherwise isogenic wild-type plants. Cellulose production in the transgenic plants is shown to be significantly reduced compared to wild-type plants. The severity of phenotype of the transgenic plants thus produced varies considerably, depending to some extent upon the level of inhibition of cellulose biosynthesis.

10

TABLE 9

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LEVELS OF ANTISENSE GENE EXPRESSION AND FERTILITY IN T1 LINES OF ANTISENSE 35S-RSW1 PLANTS

| 5 | TI PLANT LINE | ANTISENSE 35S- <i>RSW</i> 1 EXPRESSION | FERTILITY | T1 PLANT LINE | ANTISENSE 35S-RSW1 EXPRESSION | FERTILITY |
|----|---------------------|--|-----------|---------------------|-------------------------------|-----------|
| | В | very high | sterile* | 2H | medium | fertile |
| | 2B | very high | sterile* | С | medium | sterile* |
| | 3E | very high | fertile | F | medium | sterile* |
| 10 | 2E | high | sterile* | 2Q | medium | fertile |
| | 2K | high | sterile* | 3P | medium | sterile* |
| | 2M | high | sterile* | 3T | medium | fertile |
| | 20 | high | sterile* | 5D | medium | sterile* |
| | 2P | high | sterile* | 6A | medium | fertile |
| 15 | 2W | high | fertile | 8E | low | fertile |
| | 2Z | high | sterile* | 2R | low | sterile* |
| | 3G | high | sterile* | 7A | low | fertile |
| | 3Q | high | sterile* | 7 S | low | fertile |
| | 7Q | high | sterile* | 70 | low | fertile |
| 20 | 7N | medium | sterile* | 7R | low | fertile |
| | 7G | medium | fertile | 1B | very low | fertile |
| | 1C | medium | sterile* | 2 U | very low | fertile |
| | 2X | medium | sterile* | | | |

^{*}sterile phenotype not indicative of complete sterility, but that hand pollination at least, is

²⁵ required to obtain seed from such plants.

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EXAMPLE 10 RSW1 RELATED SEQUENCES IN RICE PLANTS

To identify RSW1 related nucleotide sequences in rice, a genetic sequence database was searched for nucleotide sequences which were closely-related to one or more of the Arabidopsis thaliana RSW1 nucleotide sequences described in the preceding Examples. Rice EST S0542 (MAFF DNA bank, Japan) was identified, for which only a partial nucleotide sequences was available. Additionally, before the instant invention, there was no probable function attached to the rice EST S0542 sequence.

10

The present inventors have obtained the complete nucleotide sequence of clone S0542 and derived the amino acid sequence encoded therefor. The S0542 cDNA is only 1741bp in length and appears to be a partial cDNA clone because, although it comprises 100bp of 5'-untranslated sequence and contains the ATG start codon, it is truncated at 3'-end and, as a consequence encodes only the first 547 amino acid residues of the rice RSW1 or RSW1-like polypeptide. Based upon the length of the corresponding *Arabidopsis thaliana* RSW1 polypeptide (1081 amino acids), the rice RSW1 sequence set forth in SEQ ID NO:14 appears to contain approximately one-half of the complete amino acid sequence.

- The N-terminal half of the rice RSW1 amino acid sequence is approximately 70% identical to the *Arabidopsis thaliana* RSW1 polypeptide set forth in SEQ ID NO:6, with higher homology (approximately 90%) occurring between amino acid residues 271-547 of the rice sequence. These data strongly suggest that S0542 is the rice homologue of the *A. thaliana RSW*1 gene. Alignments of rice, *A. thaliana* and cotton RSW1 amino acid sequences are presented in 25 Figures 9 and 10.
- To isolate full-length cDNA clones and genomic clone equivalents of S0542 (this study and MAFF DNA bank, Japan) or D48636 (Pear et al., 1996), cDNA and genomic clone libraries are produced using rice mRNA and genomic DNA respectively, and screened by hybridisation 30 using the S0542 or D48636 cDNAs as a probe, essentially as described herein. Positive-

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hybridising plaques are identified and plaque-purified, during further rounds of screening by hybridisation, to single plaques.

The rice clones are sequenced as described in the preceding Examples to determine the complete nucleotide sequences of the rice RSW1 genes and derived amino acid sequences therefor. Those skilled in the art will be aware that such gene sequences are useful for the production of transgenic plants, in particular transgenic cereal plants having altered cellulose content and/or quality, using standard techniques. The present invention extends to all such genetic sequences and applications therefor.

10

EXAMPLE 11 RSW1 RELATED SEQUENCES IN COTTON PLANTS

15 A ³²P-labelled RSW1 PCR fragment was used to screen approximately 200,000 cDNA clones in a cotton fibre cDNA library. The RSW1 PCR probe was initially amplified from Arabidopsis thaliana wild type cDNA using the primers 2280-F and csp1-R described in the preceding Examples, and then re-amplified using the primer combination 2370-F/csp1-R, also described in the preceding Examples.

20

Hybridisations were carried out under low stringency conditions at 55°C.

Six putative positive-hybridising plaques were identified in the first screening round. Using two further rounds of screening by hybridisation, four of these plaques were purified to single plaques. Three plaques hybridise very strongly to the RSW1 probe while the fourth plaque hybridises less intensely.

We conclude that the positive-hybridising plaques which have been purified are strong candidates for comprising cotton RSW1 gene sequences or RSW1-like gene sequences.

30 Furthermore, the cotton cDNAs may encode the catalytic subunit of cellulose synthase,

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because the subunit protein architecture of cellulose synthase appears to be highly conserved among plants as highlighted in the preceding Example.

Furthermore, a Southern blot of cotton genomic DNA digested with BgIII was hybridised with 5 the 5' end of the RSW1 cDNA, under low stringency hybridisation conditions at 55°C. Results are presented in Figure 11. These data demonstrate that RSW1-related sequences exist in the cotton genome.

The cotton cDNA clones described herein are sequenced as described in the preceding 10 Examples and used to produce transgenic cotton plants having altered fibre characteristics. The cDNAs are also used to genetically alter the cellulose content and/or quality of other plants, using standard techniques.

EXAMPLE 12 RSW1 RELATED SEQUENCES IN EUCALYPTUS SSP.

Putative Eucalyptus ssp. cellulose synthase catalytic subunit gene fragments were obtained by amplification using PCR. DNA primers were designed to conserved amino acid residues found in the Arabidopsis thaliana RSW1 and 12C4 amino acid sequences. Three primers were used 20 for PCR. The primers are listed below:

pcsF-I 5'- A A/G A A G A T I G A C/T T A C/T C/T T I A A A/G G A C/T A A-3'
pcsR-II 5'-A T I G T I G G I G T I C G/T A/G T T C/T T G A/T/G/C C T/G A/T/C/G C C -3'
pcsF-II 5'- G C I A T G A A A/G A/C G I G A I T A C/T G A A/G G A -3'

25

15

Using standard PCR conditions (50°C annealing temperature) and solutions, the primer sets pcsF-I/pcsR-II and pcsF-II/pcsR-II were used to amplify genetic sequences from pooled *Eucalyptus ssp.* cDNA. In the first reaction primers pcsF-I and pcsR-II were used to generate a fragment approximately 700 bp in length. In the second PCR reaction, which used primers pcsF-II and pcsR-II, a fragment estimated to 700 bp was obtained. The sizes of the PCR

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fragments are within the size range estimated for the corresponding Arabidopsis thaliana sequences.

We conclude that the amplified *Eucalyptus ssp.* PCR fragments are likely to be related to the 5 *Arabidopsis thaliana RSW*1 gene and may encode at least a part of the *Eucalyptus ssp.* cellulose synthase catalytic subunit.

The Eucalyptus ssp. PCR clones described herein are sequenced as described in the preceding Examples and used to isolate the corresponding full-length Eucalyptus ssp cDNAs and genomic gene equivalents. Those skilled in the art will be aware that such gene sequences are useful for the production of transgenic plants, in particular transgenic Eucalyptus ssp plants having altered cellulose content and/or quality, using standard techniques. The present invention extends to all such genetic sequences and applications therefor.

15

EXAMPLE 13

NON-CRYSTALLINE B-1,4-GLUCAN AS A MODIFIER OF CELL WALL PROPERTIES

20 The properties of plant cell walls depend on the carbohydrates, proteins and other polymers of which they are composed and the complex ways in which they interact. Increasing the quantities of non-crystalline β-1,4-glucan in cell walls affects those wall properties which influence mechanical, nutritional and many other qualities as well as having secondary consequences resulting from the diversion of carbon into non-crystalline glucan at the expense of other uses. To illustrate one of these effects, we investigated the ability of the non-crystalline glucan to hydrogen bond to other wall components particularly cellulose in the way that has been shown to be important for wall mechanics.

Hemicelluloses such as xyloglucans cross-link cellulose microfibrils by hydrogen bonding to 30 the microfibril surface (Levy et al., 1991). Since the β -1,4-glucan backbone of xyloglucan is

thought to be responsible for hydrogen bonding (with the xylose, galactose and fucose substitutions limiting the capacity to form further hydrogen bonds) we can expect the non-crystalline β-1,4-glucan also to have a capacity to hydrogen bond and cross link cellulose. The effectiveness of strong alkalis in extracting xyloglucans is thought to relate to their disruption of the hydrogen bonds with cellulose (Hayashi and MacLachlan, 1984).

To demonstrate that the non-crystalline β-1,4-glucan forms similar associations with the cellulose microfibrils, we examined whether the 4 M KOH fraction, extracted from shoots of the rsw1 mutant and from wild type RSW1 plants, contained non-crystalline glucan in addition to xyloglucan. The non-crystalline glucan was separated from xyloglucan in the 4 M KOH extract by dialysing the neutralised extract against distilled water and centrifuging at 14000 g for 1 hour. The pellet was shown to be a pure β-1,4-glucan by using the methods for monosaccharide analysis, methylation analysis and enzyme digestion used to characterise the glucan in the ammonium oxalate fraction (see Example 1).

15

Table 10 shows the presence of substantial quantities of glucan recovered in pure form in the pellet from 4 M KOH fractions extracted from the overproducing rsw1 mutant of Arabidopsis thaliana. These data also demonstrate the presence of smaller quantities of non-crystalline β-1,4-glucan in the 4 M KOH fraction from wild type plants, compared to rsw1, particularly 20 when grown at 31 °C.

TABLE 10

Glucose contents* of 4M KOH fractions from shoots of wild-type and
rsw1mutant Arabidopsis thaliana plants

| | Glucose fraction | wild | -type | rsw1 r | nutant |
|----|----------------------------------|------|-------|--------|--------|
| | | 21°C | 31°C | 21°C | 31°C |
| 25 | xyloglucan and non-crystalline | | | | |
| | glucan in whole extract | 36.4 | 56.9 | 27.1 | 93.1 |
| | non-crystalline glucan in pellet | 7.8 | 20.5 | 7.6 | 56.0 |

^{*,} nmol glucose/ mg plant dry weight after TFA hydrolysis

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The monosaccharide composition of the supernatant remaining after centrifugation was determined after TFA hydrolysis. These data, and data from methylation analysis, are consistent with the supernatant being a relatively pure xyloglucan. The supernatant was free of glucan, because no glucose could be released by the endocellulase/β-glucosidase mixture that released glucose from β-1,4-glucan.

The presence of both non-crystalline β -1,4-glucan and xyloglucan in the 4 M KOH fraction, when taken together with the implications from structural predictions (Levy *et al*, 1991), is consistent with some of the non-crystalline β -1,4-glucan in the wall hydrogen bonding to 10 cellulose microfibrils in similar fashion to the β -1,4-glucan backbone of xyloglucan.

The cross linking provided when xyloglucans and other hemicelluloses bind to two or more microfibrils is an important determinant of the mechanical properties of cellulosic walls (Hayashi, 1989). The effects of increasing the amounts of non-crystalline β-1,4-glucan in walls are likely to be greatest in walls which otherwise possess relatively low levels of cross linking as a result of high ratios of cellulose: hemicelluloses. Such conditions are common in secondary walls including those of various fibres, and the cellulose:hemicellulose ratio is particularly high in cotton fibres.

20 The effects on wall mechanical properties of overproducing non-crystalline glucan are shown by transforming plants with the mutant allele of rswl (SEQ ID NO:11) operably under the control of either the RSW1 promoter derived from SEQ ID NO:3 or SEQ ID NO:4 or alternatively, an appropriate constitutive promoter such as the CaMV 35S promoter. Production of non-crystalline glucan is quantified by fractionating the cell walls using the methods described above to show in particular that non-crystalline glucan is recovered in the 4 M KOH fraction. Mechanical properties of the cell walls are measured using standard methods for fibre analysis to study parameters such as stress-strain curves, and breaking strain, amongst other properties.

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EXAMPLE 14 OVER-EXPRESSION OF CELLULOSE SYNTHASE IN TRANSGENIC PLANTS

5 Three strategies are employed to over-express cellulose synthase in *Arabidopsis thaliana* plants.

In the first strategy, the CaMV 35S promoter sequence is operably connected to the full-length cellulose synthase cDNA which is obtainable by primer extension of SEQ ID NO:1. This is achievable by cloning the full-length cDNA encoding cellulose synthase, in the sense orientation, between the CaMV 35S promoter or other suitable promoter operable in plants and the nopaline synthase terminator sequences of the binary plasmid pBI121.

In the second strategy, the coding part of the genomic gene is cloned, in the sense orientation, between the CaMV 35S promoter and the nopaline synthase terminator sequences of the binary plasmid pBI121.

In the third strategy, the 23H12 binary cosmid clone or the derivative pRSW1, containing the cellulose synthase gene sequence operably under the control of the cellulose synthase gene promoter and terminator sequences is prepared in a form suitable for transformation of plant tissue.

For Agrobacterium-mediated tissue transformation, binary plasmid constructs discussed supra are transformed into Agrobacterium tumefaciens strain AGL1 or other suitable strain. The recombinant DNA constructs are then introduced into wild type Arabidopsis thaliana plants (Columbia ecotype), as described in the preceding Examples.

Alternatively, plant tissue is directly transformed using the vacuum infiltration method described by Beshtold et al. (1993).

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The transgenic plants thus produced exhibit a range of phenotypes, partly because of position effects and variable levels of expression of the cellulose synthase transgene.

Cellulose content in the transgenic plants and isogenic untransformed control plants is determined by the ¹⁴C incorporation assay or as acetic/nitric acid insoluble material as described in Example 1. In general, the level of cellulose deposition and rates of cellulose biosynthesis in the transgenic plants are significantly greater than for untransformed control plants.

10 Furthermore, in some cases, co-supression leads to mimicry of the rswl mutant phenotype.

EXAMPLE 15 SITE-DIRECTED MUTAGENESIS OF THE RSW1 GENE

15

The nucleotide sequence of the RSW1 gene contained in 23H12 is mutated using site-directed mutagenesis, at several positions to alter its catalytic activity or substrate affinity or glucan properties. In one example, the RSW1 gene is mutated to comprise one or more mutations present in the mutant rsw1 allele.

20

The mutated genetic sequences are cloned into binary plasmid described in the preceding Examples, in place of the wild-type sequences. Plant tissue obtained from both wild-type Arabidopsis thaliana (Columbia) plants and A. thaliana rswl plants is transformed as described herein and whole plants are regenerated.

25

Control transformations are performed using the wild-type cellulose synthase gene sequence.

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EXAMPLE 16

PHENOTYPES OF PLANTS EXPRESSING MUTATED RSW1 GENES

Plants transformed with genetic constructs described in Example 15 (and elsewhere) are categorised initially on the basis of number of transgene copies, to eliminate variability arising therefrom. Plants expressing single copies of different transgenes are analysed further for cell wall components, including cellulose, non-crystalline β-1,4-glucan polymer, starch and carbohydrate content.

10 1. Cellulose content

Cellulose content in the transgenic plants is determined by the ¹⁴C incorporation assay as described in Example 1. Cell walls are prepared, fractionated and the monosaccharide composition of individual fractions determined as in Example 1.

15 2. Non-crystalline β-1,4-glucan content

Transgenic plants expressing the rsw1 mutant allele exhibit a higher level of non-crystalline, and therefore extractable, β -1,4-glucan in cell walls compared to plants expressing an additional copy of the wild-type RSW1 allele. Thus, it is possible to change the crystallinity of the β -1,4-glucan chains present in the cell wall by mutation of the wild-type RSW1 allele.

20

3. Starch content

Transgenic plants are also analysed to determine the effect of mutagenesis of the RSW1 gene on the level of starch deposited in their roots. The quantity of starch present in material prepared from the crude wall fraction is determined using the anthrone/H₂SO₄ method described in Example 1. The data show that mutating the RSW1 gene to the mutant rsw1 allele increases starch deposition. This demonstrates that the gene can be used to alter the partitioning of carbon into carbohydrates other than cellulose.

4.Cell wall composition

30 The cell wall composition of transgenic plant material is also analysed. Wild type and rswl

and transgenic seedlings are grown for 2 d at 21°C and then kept for a further 5 d at either 21°C or 31°C. With transfer to 31°C when the seed has scarcely germinated, the wall composition at final harvest largely reflects the operation of the mutated rsw1 gene product at its restrictive temperature. Cell wall fractionation is carried out in similar fashion to that described for the ¹⁴C-experiment (Example 1) and the monosaccharide composition of each fraction is quantified by GC/MS after hydrolysis with trifluoroacetic acid or, in the case of crystalline cellulose, H₂SO₄.

In some transgenic plants in which the RSW1 gene is mutated, the monosaccharide 10 composition is comparable to that observed for homozygous rsw1 plants, at least in some cases, confirming that there is a major reduction in the quantity of crystalline cellulose in the final, acid insoluble fraction. Thus, mutation of the RSW1 gene can be performed to produce changes in the composition of plant cell walls.

15 EXAMPLE 17

CHEMICAL MODIFICATION OF THE RSWI GENE TO MANIPULATE CELLULOSE PRODUCTION AND PLANT CELL WALL CONTENT.

As demonstrated in the preceding Examples, the RSW1 gene is involved in cellulose 20 production and the manipulation of cell wall content.

In the present Example, to identify novel phenotypes and gene sequences important for the normal functioning of the cellulose synthase gene, the RSW1 gene is modified in planta, using the chemical mutagen EMS. The mutant plants are identified following germination and the modified RSW1 genes are isolated and characterised at the nucleotide sequence level. A sequence comparison between the mutant gene sequences and the wild type sequence reveals nucleotides which encode amino acids important to the normal catalytic activity of the cellulose synthase enzyme, at least in Arabidopsis thaliana plants.

30 This approach thus generates further gene sequences of utility in the modification of cellulose

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content and properties in plants.

EXAMPLE 18

DISCUSSION

5

Five pieces of evidence make a compelling case that the RSW1 gene product encodes the catalytic subunit of cellulose synthase:

- 1. The rsw1 mutation selectively inhibits cellulose synthesis and promotes accumulation of a non-crystalline β -1,4-glucan;
- 10 2. The rsw1 mutation removes cellulose synthase complexes from the plasma membrane, providing a plausible mechanism for reduced cellulose accumulation and placing the RSW1 product either in the complexes or interacting with them;
 - 3. The D,D,D,QXXRW signature identifies the RSW1 gene product as a processive glycosyl transferase enzyme (Saxena, 1995);
- 15 4. The wild type allele corrects the temperature sensitive phenotype of the rsw1 mutant; and
 - 5. Antisense expression of the RSW1 in transgenic plants grown at 21 °C reproduces some of the phenotype of rsw1 which is observed following growth at 31 °C.
- 20 Consistent with the plasma membrane location expected for a catalytic subunit, the putative 122 kDa RSW1 product contains 8 predicted membrane-spanning regions. Six of these regions cluster near the C-terminus (Figure 10), separated from the other two by a domain that is probably cytoplasmic and has the weak sequence similarities to prokaryotic glycosyl transferases (Wong, 1990; Saxena, 1990; Matthyse, 1995; Sofia, 1994; Kutish, 1996).

25

RSW1 therefore qualifies as a member of the large family of *Arabidopsis thaliana* genes whose members show weak similarities to bacterial cellulose synthase. RSW1 is the first member of that family to be rigorously identified as an authentic cellulose synthase. Among the diverse genes in *A. thaliana*, at least two genes show very strong sequence similarities to 30 the *RSW*1 gene and are most likely members of a highly conserved sub-family involved in

cellulose synthesis. The closely related sequences come from cosmid 12C4, a partial genomic clone cross-hybridising with EST T20782 designated *Ath*-A, and from a full length cDNA designated *Ath*-B.

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5 Ath-A resembles RSW1 (SEQ ID NO:5) at its N-terminus whereas Ath-B starts 22 amino acid residues downstream [Figure 8 and Figure 9(i), (ii) and (iii)]. Closely related sequences in other angiosperms are the rice EST S0542 [Figure 9(i), (ii) and (iii)], which resembles the polypeptides encoded by RSW1 and Ath-A and the cotton celA1 gene (Pear, 1996) at the N-terminus.

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The Arabidopsis thaliana, rice and cotton genes have regions of very high sequence similarity interspersed with variable regions (Figures 9 and 10). Most of the highest conservation among those gene products occurs in their central cytoplasmic domain where the weak similarities to the bacterial cellulose synthase occur. The N-terminal region that precedes the first 15 membrane spanning region is probably also cytoplasmic but shows many amino acid substitutions as well as sequences in RSW1 that have no counterpart in some of the other genes as already noted for celA. An exception to this is a region comprising 7 cysteine residues with highly conserved spacings (Figure 10). This is reminiscent of regions suggested to mediate protein-protein and protein-lipid interactions in diverse proteins including 20 transcriptional regulators and may account for the striking sequence similarity between this region of RSW1 and two putative soybean bZIP transcription factors (Genbank SOYSTF1A and 1B).

In conclusion, the chemical and ultrastructural changes seen in the cellulose-deficient mutant combine with gene cloning and complementation of the mutant to provide strong evidence that the RSW1 locus encodes the catalytic subunit of cellulose synthase. Accumulation of non-crystalline β-1,4-glucan in the shoot of the rsw1 mutant suggests that properties affected by the mutation are required for glucan chains to assemble into microfibrils. Whilst not being bound by any theory or mode of action, a key property may be the aggregation of catalytic subunits into plasma membrane rosettes. At the restrictive temperature, mutant synthase

complexes disassemble to monomers (or smaller oligomers) that are undetectable by freeze etching. At least in the shoot, the monomers seem to remain biosynthetically active but their β-1,4-glucan products fail to crystallise into microfibrils probably because the chains are growing from dispersed sites. Crystallisation into microfibrils, with all its consequences for wall mechanics and morphogenesis, therefore may depend upon catalytic subunits remaining aggregated as plasma membrane rosettes.

Those skilled in the art will appreciate that the invention described herein is susceptible to variations and modifications other than those specifically described. It is to be understood that the invention includes all such variations and modifications. The invention also includes all of the steps, features, compositions and compounds referred to or indicated in this specification, individually or collectively, and any and all combinations or any two or more of said steps or features.

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SEQUENCE LISTING

(1) GENERAL INFORMATION: 5 (i) APPLICANT: Australian National University and the Commonwealth Scientific and Industrial Research Organisation 10 (ii) TITLE OF INVENTION: Manipulation of plant cellulose (iii) NUMBER OF SEQUENCES: 14 (iv) CORRESPONDENCE ADDRESS: 15 (A) ADDRESSEE: Davies Collison Cave Patent Attorneys (B) STREET: 1, Little Collins Street (C) CITY: Melbourne (D) STATE: Victoria (E) COUNTRY: Australia 20 (F) ZIP: 3000 (v) COMPUTER READABLE FORM: (A) MEDIUM TYPE: Floppy disk (B) COMPUTER: IBM PC compatible 25 (C) OPERATING SYSTEM: PC-DOS/MS-DOS (D) SOFTWARE: PatentIn Release #1.0, Version #1.25 (vi) CURRENT APPLICATION DATA: (A) APPLICATION NUMBER: PCT INTERNATIONAL 30 (B) FILING DATE: (vii) PRIOR APPLICATION DATA: (A) APPLICATION NUMBER: AU PO0699 (B) FILING DATE: 27-JUN-1996 35 (viii) ATTORNEY/AGENT INFORMATION: (A) NAME: SLATTERY, JOHN M (ix) TELECOMMUNICATION INFORMATION: 40 (A) TELEPHONE: 61-3-9254-2777

(B) TELEFAX: 61-3-9254-2770

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(C) TELEX: AA31787 (2) INFORMATION FOR SEQ ID NO:1: 5 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 2248 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear 10 (ii) MOLECULE TYPE: cDNA (iii) HYPOTHETICAL: NO 15 (vi) ORIGINAL SOURCE: (A) ORGANISM: Arabidopsis thaliana (vii) IMMEDIATE SOURCE: (B) CLONE: EST T20782 20 (ix) FEATURE: (A) NAME/KEY: CDS (B) LOCATION: 1..1887 25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:1: CGA GCT ATG AAG AGA GAG TAT GAA GAG TTT AAA GTG AGG ATA AAT GCT 48 Arg Ala Met Lys Arg Glu Tyr Glu Glu Phe Lys Val Arg Ile Asn Ala 30 ı 5 10 15 CTT GTT GCC AAA GCA CAG AAA ATC CCT GGA GAA GGC TGG ACA ATG CAG 96 Leu Val Ala Lys Ala Gln Lys Ile Pro Gly Glu Gly Trp Thr Met Gln 20 25 30 35

GAT GGT ACT CCC TGG CCT GGT AAC AAC ACT AGA GAT CAT CCT GGA ATG

Asp Gly Thr Pro Trp Pro Gly Asn Asn Thr Arg Asp His Pro Gly Met

45

40

35

144

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| | ATA | CAG | GTG | TTC | TTA | GGC | CAT | AGT | GGG | GGT | CTG | GAT | ACC | GAT | GGA | AAT | נ | 92 |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|---|-----|
| | Ile | Gln | Val | Phe | Leu | Gly | His | Ser | Gly | Gly | Leu | Asp | Thr | qaA | Gly | Asn | | |
| | | 50 | | | | | 55 | | | | | 60 | | | | | | |
| | | | | | | | | | | | | | | | | | | |
| 5 | GAG | CTG | CCT | AGA | CTC | ATC | TAT | GTT | TCT | CGT | GAA | AAG | CGG | CCT | GGA | TTT | 2 | 240 |
| | Glu | Leu | Pro | Arg | Leu | Ile | Tyr | Val | Ser | Arg | Glu | Lys | Arg | Pro | Gly | Phe | | |
| | 65 | | | | | 70 | | | | | 75 | | | | | 80 | | |
| | | | | | | | | | | | | | | | | | | |
| | CAA | CAC | CAC | AAA | AAG | GCT | GGA | GCT | ATG | AAT | GCA | TCG | ATC | CGT | GTA | TCT | 2 | 889 |
| 10 | Gln | His | His | Lys | Lys | Ala | Gly | Ala | Met | Asn | Ala | Ser | Ile | Arg | Val | Ser | | |
| | | | | | 85 | | | | | 90 | | | | | 95 | | | |
| | | | | | | | | | | | | | | | | | | |
| | GCT | GTT | CTT | ACC | AAT | GGA | GCA | TAT | CTT | TTG | AAC | GTG | GAT | TGT | GAT | CAT | 3 | 336 |
| | Ala | Val | Leu | Thr | Asn | Gly | Ala | Tyr | Leu | Leu | Asn | Val | Asp | Cys | Asp | His | | |
| 15 | | | | 100 | | | | | 105 | | | | | 110 | | | | |
| | | | | | | | | | | | | | | | | | | |
| | TAC | TTT | AAT | AAC | AGT | AAG | GCT | ATT | AAA | GAA | GCT | ATG | TGT | TTC | ATG | ATG | 3 | 384 |
| | Tyr | Phe | Asn | Asn | Ser | Lys | Ala | Ile | Lys | Glu | Ala | Met | Cys | Phe | Met | Met | | |
| | | | 115 | | | | | 120 | | | | | 125 | | | | | |
| 20 | | | | | | | | | | | | | | | | | | |
| | GAC | CCG | GCT | ATT | GGA | AAG | AAG | TGC | TGC | TAT | GTC | CAG | TTC | CCT | CAA | CGT | 4 | 132 |
| | Asp | Pro | Ala | Ile | Gly | Lys | Lys | Сув | Cys | Tyr | Val | Gln | Phe | Pro | Gln | Arg | | |
| | | 130 | | | | | 135 | | | | | 140 | | | | | | |
| | | | | | | | | | | | | | | | | | | |
| 25 | TTT | GAC | GGT | ATT | GAT | TTG | CAC | GAT | CGA | TAT | GCC | AAC | AGG | AAT | ATA | GTC | 4 | 80 |
| | Phe | Asp | Gly | Ile | Asp | Leu | His | qaA | Arg | Tyr | Ala | Asn | Arg | Asn | Ile | Val | | |
| | 145 | | | | | 150 | | | | | 155 | | | | | 160 | | |
| | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | CCA | | 9 | 528 |
| 30 | Phe | Phe | Asp | Ile | Asn | Met | Lys | Gly | Leu | Asp | Gly | Ile | His | Gly | Pro | Val | | |
| | | | | | 165 | | | | | 170 | | | | | 175 | | | |
| | | | | | | | | | | | | | | | | | | |
| | TAT | GTG | GGT | ACT | GGT | TGT | TGT | TTT | AAT | AGG | CAG | GCT | CTA | TAT | GGG | TAT | 5 | 576 |
| | Tyr | Val | Gly | Thr | Gly | Cys | Сув | Phe | Asn | Arg | Gln | Ala | Leu | Tyr | Gly | Tyr | | |
| 35 | | | | 180 | | | | | 185 | | | | | 190 | | | | |
| | | | | | | | | | | | | | | | | | | |
| | GAT | CCT | GTT | TTG | ACG | GAA | GAA | GAT | TTA | GAA | CCA | AAT | ATT | ATT | GTC | AAG | • | 624 |
| | qaA | Pro | Val | Leu | Thr | Glu | Glu | qaA | Leu | Glu | Pro | Asn | Ile | Ile | Val | Lys | | |
| | | | 195 | | | | | 200 | | | | | 205 | | | | | |
| 40 | | | | | | | | | | | | | | | | | | |

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| | AGC | TGT | TGC | GGG | TCA | AGG | AAG | AAA | GGT | AAA | AGT | AGC | AAG | AAG | TAT | AAC | 672 |
|-----|------|------|-----|------------|-------------|-----|-------|------|------|-----|-----|-----|-----|----------|-----|------|------|
| | Ser | Cys | Сув | Gly | Ser | Arg | Lys | Lys | Gly | Lys | Ser | Ser | Lys | Lys | Tyr | Asn | |
| | | 210 | | | | | 215 | | | | | 220 | | | | | |
| | | | | | | | | | | | | | | | | | |
| 5 | TAC | GAA | AAG | AGG | AGA | GGC | ATC | AAC | AGA | AGT | GAC | TCC | AAT | GCT | CCA | CTT | 720 |
| | Tyr | Glu | Lys | Arg | Arg | Gly | Ile | Asn | Arg | Ser | qeA | Ser | Asn | Ala | Pro | Leu | |
| | 225 | | | | | 230 | | | | | 235 | | | | | 240 | |
| | | | | | | | | | | | | | | | | | |
| • ^ | | | | GAG | | | | | | | | | | | | | 768 |
| 10 | Phe | Asn | Met | Glu | | Ile | Asp | Glu | Gly | | Glu | Gly | Tyr | Asp | | Glu | |
| | | | | | 245 | | | | | 250 | | | | | 255 | | |
| | NCC. | mar. | እጥጥ | C/Tr N | N.T.C | maa | C n C | NCC. | NCT. | CTA | CNC | 220 | CCT | an areas | COM | CNC | 916 |
| | | | | CTA | | | | | | | | | | | | | 816 |
| 15 | Arg | 261 | 116 | Leu 260 | MEL | 261 | GIII | MIG | 265 | vai | GIU | гу | ALY | 270 | GIY | GIII | |
| 1 3 | | | | 200 | | | | | 203 | | | | | 270 | | | |
| | TCG | ccc | GTA | TTT | ል ጥጥ | GCG | GCZ | ልሮሮ | ידיר | ATG | GAA | CDD | GGC | GGC | ውጥ | CCA | 864 |
| | | | | Phe | | | | | | | | | | | | | |
| | | | 275 | | | | | 280 | | | | | 285 | , | | | |
| 20 | | | | | | | | | | | | | | | | | |
| | CCA | ACA | ACC | AAT | ccc | GCT | ACT | СТТ | CTG | AAG | GAG | GCT | ATT | CAT | GTT | ATA | 912 |
| | Pro | Thr | Thr | Asn | Pro | Ala | Thr | Leu | Leu | Lys | Glu | Ala | Ile | His | Val | Ile | |
| | | 290 | | | | | 295 | | | | | 300 | | | | | |
| | | | | | | | | | | | | | | | | | |
| 25 | AGC | TGT | GGT | TAC | GAA | GAC | AAG | ACT | GAA | TGG | GGC | AAA | GAG | ATT | GGT | TGG | 960 |
| | Ser | Cys | Gly | Tyr | Glu | Asp | Lys | Thr | Glu | Trp | Gly | Lys | Glu | Ile | Gly | Trp | |
| | 305 | | | | | 310 | | | | | 315 | | | | | 320 | |
| | | | | | | | | | | | | | | | | | |
| | | | | TCC | | | | | | | | | | | | | 1008 |
| 30 | Ile | Tyr | Gly | Ser | Val | Thr | Glu | Asp | Ile | Leu | Thr | Gly | Phe | Lув | Met | His | |
| | | | | | 325 | | | | | 330 | | | | | 335 | | |
| | | | | | | | | | | | | | | | | | |
| | _ | | _ | TGG | _ | | _ | | | | | | | | | | 1056 |
| 25 | Ala | Arg | Gly | Trp | Ile | Ser | Ile | Tyr | • | Asn | Pro | Pro | Arg | | Ala | Phe | |
| 35 | | | | 340 | | | | | 345 | | | | | 350 | | | |
| | 220 | cor | mc~ | cc* | 001 | 200 | 225 | ~~~ | m~ | a.~ | | m | | | - | - | |
| | | | | GCA | | | | | | | | | | | | | 1104 |
| | ъÀа | GIĀ | | Ala | Pro | 116 | nsa | | ser | Asp | arg | red | | GIN | val | ьeu | |
| | | | 355 | | | | | 360 | | | | | 365 | | | | |

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| | CGA | TGG | GCT | TTG | GGA | TCT | ATC | GAG | TTA | CTT | CTT | AGC | AGA | CAT | TGT | CCT | 1152 |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
| | Arg | Trp | Ala | Leu | Gly | Ser | lle | Glu | Ile | Leu | Leu | Ser | Arg | His | Суз | Pro | |
| | | 370 | | | | | 375 | | | | | 380 | | | | | |
| | | | | | | | | | | | | | | | | | |
| 5 | ATC | TGG | TAT | GGT | TAC | CAT | GGA | AGG | TTG | AGA | CTT | TTG | GAG | AGG | ATC | GCT | 1200 |
| | Ile | Trp | Tyr | Gly | Tyr | His | Gly | Arg | Leu | Arg | Leu | Leu | Glu | Arg | Ile | Ala | |
| | 385 | | | | | 390 | | | | | 395 | | | | | 400 | |
| | | | | | | | | | | | | | | | | | |
| | TAT | ATC | AAC | ACC | ATC | GTC | TAT | CCT | ATT | ACA | TCC | ATC | CCT | CTT | ATT | GCG | 1248 |
| 10 | Tyr | Ile | Asn | Thr | Ile | Val | Tyr | Pro | Ile | Thr | Ser | Ile | Pro | Leu | Ile | Ala | |
| | | | | | 405 | | | | | 410 | | | | | 415 | | |
| | | | | | | | | | | | | | | | | | |
| | TAT | TGT | ATT | CTT | CCC | GCT | TTT | TGT | CTC | ATC | ACC | GAC | AGA | TTC | ATC | ATA | 1296 |
| | Tyr | Cys | Ile | Leu | Pro | Ala | Phe | Сув | Leu | Ile | Thr | Asp | Arg | Phe | Ile | Ile | |
| 15 | | | | 420 | | | | | 425 | | | | | 430 | | | |
| | | | | | | | | | | | | | | | | | |
| | ccc | GAG | ATA | AGC | AAC | TAC | GCG | AGT | ATT | TGG | TTC | ATT | CTA | CTC | TTC | ATC | 1344 |
| | Pro | Glu | Ile | Ser | Asn | Tyr | Ala | Ser | Ile | Trp | Phe | Ile | Leu | Leu | Phe | Ile | |
| | | | 435 | | | | | 440 | | | | | 445 | | | | |
| 20 | | | | | | | | | | | | | | | | | |
| | TCA | ATT | GCT | GTG | ACT | GGA | ATC | CTG | AAA | CTG | AAA | TGG | AAC | GGT | GTG | AGC | 1392 |
| | Ser | Ile | Ala | Val | Thr | Gly | Ile | Leu | Lys | Leu | Lys | Trp | Asn | Gly | Val | Ser | |
| | | 450 | | | | | 455 | | | | | 460 | | | | | |
| | | | | | | | | | | | | | | | | | |
| 25 | ATT | GAG | GAT | TGG | TGG | AGG | AAC | AAC | CAG | TTC | TGG | GTC | ATT | GGT | GGC | ACA | 1440 |
| | Ile | Glu | Asp | Trp | Trp | Arg | Asn | Asn | Gln | Phe | Trp | Val | Ile | Gly | Gly | Thr | |
| | 465 | | | | | 470 | | | | | 475 | | | | | 480 | |
| | | | | | | | | | | | | | | | | | |
| | TCC | ACC | CAT | CTT | TTT | GCT | GTC | TTC | CAA | GGT | CTA | CTT | AAG | GTT | CTT | GCT | 1488 |
| 30 | Ser | Thr | His | Leu | Phe | Ala | Val | Phe | Gln | Gly | Leu | Leu | Lys | Val | Leu | Ala | |
| | | | | | 485 | | | | | 490 | | | | | 495 | | |
| | | | | | | | | | | | | | | | | | |
| | GGT | ATC | AAC | ACC | AAC | TTC | ACC | GTT | ACA | TCT | AAA | GCC | ACA | AAC | AAA | AAT | 1536 |
| | Gly | Ile | Asn | Thr | Asn | Phe | Thr | Val | Thr | Ser | Lys | Ala | Thr | Asn | Lys | Asn | |
| 35 | | | | 500 | | | | | 505 | | | | | 510 | | | |
| | | | | | | | | | | | | | | | | | |
| | GGG | GAT | TTT | GCA | AAA | СТС | TAC | ATC | TTC | AAA | TGG | ACA | GCT | CTT | CTC | ATT | 1584 |
| | Gly | Asp | Phe | Ala | Lys | Leu | Tyr | Ile | Phe | Lys | Trp | Thr | Ala | Leu | Leu | Ile | |
| | | | 515 | | | | | 520 | | | | | 525 | | | | |
| 40 | | | | | | | | | | | | | | | | | |

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| | CCA | CCA | ACC | ACC | GTC | CTA | CTT | GTG | AAC | CTC | ATA | GGC | ATT | GTG | GCT | GGT | 1632 |
|----|-----|-------|-------|-------|-------|-------|------|-------|--------|-------|------|-------|-------------|-------|-------|--------|------|
| | Pro | Pro | Thr | Thr | Val | Leu | Leu | Val | neA | Leu | Ile | Gly | Ile | Val | Ala | Gly | |
| | | 530 | | | | | 535 | | | | | 540 | | | | | |
| | | | | | | | | | | | | | | | | | |
| 5 | GTC | TCT | TAT | GCT | GTA | AAC | AGT | GGC | TAC | CAG | TCG | TGG | GGT | CCG | CTT | TTC | 1680 |
| | Val | Ser | Tyr | Ala | Val | Asn | Ser | Gly | Tyr | Gln | Ser | Trp | Gly | Pro | Leu | Phe | |
| | 545 | | | | | 550 | | | | | 555 | | | | | 560 | |
| | | | | | | | | | | | | | | | | | |
| | GGG | AAG | CTC | TTC | TTC | GCC | TTA | TGG | GTT | ATT | GCC | CAT | CTC | TAC | CCT | TTC | 1728 |
| 10 | Gly | Lys | Leu | Phe | Phe | Ala | Leu | Trp | Val | Ile | Ala | His | Leu | Tyr | Pro | Phe | |
| | | | | | 565 | | | | | 570 | | | | | 575 | | |
| | | | | | | | | | | | | | | | | | |
| | TTG | AAA | GGT | CTG | TTG | GGA | AGA | CAA | AAC | CGA | ACA | CCA | ACC | ATC | GTC | TTA | 1776 |
| | Leu | Lys | Gly | Leu | Leu | Gly | Arg | Gln | Asn | Arg | Thr | Pro | Thr | Ile | Val | Ile | |
| 15 | | | | 580 | | | | | 585 | | | | | 590 | | | |
| | | | | | | | | | | | | | | | | | |
| | GTC | TGG | TCT | GTT | CTT | CTC | GCC | TCC | ATC | TTC | TCG | TTG | CTT | TGG | GTC | AGG | 1824 |
| | Val | Trp | Ser | Val | Leu | Leu | Ala | Ser | Ile | Phe | Ser | Leu | Leu | Trp | Val | Arg | |
| | | | 595 | | | | | 600 | | | | | 605 | | | | |
| 20 | | | | | | | | | | | | | | | | | |
| | ATC | AAT | ccc | TTT | GTG | GAC | GCC | AAT | ccc | AAT | GCC | AAC | AAC | TTC | AAT | GGC | 1872 |
| | Ile | Asn | Pro | Phe | Val | Asp | Ala | Asn | Pro | Asn | Ala | Asn | Asn | Phe | Asn | Gly | |
| | | 610 | | | | | 615 | | | | | 620 | | | | | |
| | | | | | | | | | | | | | | | | | |
| 25 | AAA | GGA | GGT | GTC | TTT | TAG | ACCC | TAT : | TATI | ATAC: | rt g | rgtg' | rgca' | r at | ATCA | AAAA | 1927 |
| | Lys | Gly | Gly | Val | Phe | | | | | | | | | | | | |
| | 625 | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | |
| | CGC | CAA' | TGG (| GAAT' | TCCA | AA TO | CATC | TAAA: | c ca | ATCA | AACC | CCA | GTGA | ACC (| GGGC | AGTTAA | 1987 |
| 30 | | | | | | | | | | | | | | | | | |
| | GGT | SATT | CCA ' | TGTC | CAAG | AT TA | AGCT | TTCT | C CG | AGTA | 3CCA | GAG | AAGG' | IGA . | AATT(| GTTCGT | 2047 |
| | | | | | | | | | | | | | | | | | |
| | AAC | ACTA' | TTG ' | TAAT | GATT | IT C | CAGT | GGGG | A AG | AAGA' | rgtg | GAC | CAA | ATG 2 | ATAC | ATAGTC | 2107 |
| | | | | | | | | | | | | | | | | | |
| 35 | TAC | AAAA | AGA A | ATTA | GTTA' | TA A | TTT | CTTA: | T AT | TAT' | TTTA | TTT | AAAG | CTT (| GTTA | GACTCA | 2167 |
| | | | | | | | | | | | | | | | | | |
| | CAC | TAT | GTA 2 | ATGT' | TGGA | AC T | IGTT | GTCC: | I AA I | AAAG | GAT | TGG | AGTT | rtc ' | TTTT | TATCTA | 2227 |
| | | | | | | | | | | | | | | | | | |
| | AGA | ATCT(| GAA (| GTTT | TATA | GC T | | | | | | | | | | | 2248 |
| | | | | | | | | | | | | | | | | | |

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| (2) INFORMATION FOR SEQ ID 1 | NO:Z: |
|------------------------------|-------|
|------------------------------|-------|

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 629 amino acids

5 (B) TYPE: amino acid

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

Arg Ala Met Lys Arg Glu Tyr Glu Glu Phe Lys Val Arg Ile Asn Ala 1 5 10 15

15 Leu Val Ala Lys Ala Gln Lys Ile Pro Gly Glu Gly Trp Thr Met Gln
20 25 30

Asp Gly Thr Pro Trp Pro Gly Asn Asn Thr Arg Asp His Pro Gly Met
35 40 45

20

Ile Gln Val Phe Leu Gly His Ser Gly Gly Leu Asp Thr Asp Gly Asn
50 55 60

Glu Leu Pro Arg Leu Ile Tyr Val Ser Arg Glu Lys Arg Pro Gly Phe 25 65 70 75 80

Gln His His Lys Lys Ala Gly Ala Met Asn Ala Ser Ile Arg Val Ser 85 90 95

30 Ala Val Leu Thr Asn Gly Ala Tyr Leu Leu Asn Val Asp Cys Asp His

Tyr Phe Asn Asn Ser Lys Ala Ile Lys Glu Ala Met Cys Phe Met Met
115 120 125

35

Asp Pro Ala Ile Gly Lys Lys Cys Cys Tyr Val Gln Phe Pro Gln Arg 130 135 140

Phe Asp Gly Ile Asp Leu His Asp Arg Tyr Ala Asn Arg Asn Ile Val 40 145 150 155 160

| | Phe | Phe | Asp | Ile | Asn 165 | Met | Lys | Gly | Leu | Asp 170 | Gly | Ile | His | Gly | Pro 175 | Va] |
|----|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| 5 | Tyr | Val | Gly | Thr 180 | Gly | Cys | Cys | Phe | Asn 185 | Arg | Gln | Ala | Leu | Tyr 190 | Gly | Туг |
| | Asp | Pro | Val 195 | Leu | Thr | Glu | Glu | Asp 200 | Leu | Glu | Pro | Asn | Ile 205 | Ile | Val | Lys |
| 10 | Ser | Cys 210 | Cys | Gly | Ser | Arg | Lys 215 | Lys | Gly | Lys | Ser | Ser 220 | Lys | Lys | Tyr | Asr |
| 15 | Tyr 225 | Glu | Lys | Arg | Arg | Gly 230 | Ile | Asn | Arg | Ser | Авр 235 | Ser | Asn | Ala | Pro | Le: |
| 13 | Phe | Asn | Met | Glu | Asp 245 | Ile | Авр | Glu | Gly | Phe 250 | Glu | Gly | Tyr | Asp | Авр 255 | Glu |
| 20 | Arg | Ser | Ile | Leu 260 | Met | Ser | Gln | Arg | Ser 265 | Val | Glu | Lys | Arg | Phe 270 | Gly | Glr |
| | Ser | Pro | Val 275 | Phe | Ile | Ala | Ala | Thr 280 | Phe | Met | Glu | Gln | Gly 285 | Gly | Ile | Pro |
| 25 | Pro | Thr 290 | Thr | Asn | Pro | Ala | Thr 295 | Leu | Leu | Lys | Glu | Ala 300 | Ile | His | Val | Ile |
| 20 | Ser 305 | Cys | Gly | Tyr | Glu | Asp 310 | Lys | Thr | Glu | Trp | Gly 315 | Lys | Glu | Ile | Gly | Trp 320 |
| 30 | Ile | Tyr | Gly | Ser | Val 325 | Thr | Glu | Asp | Ile | Leu 330 | Thr | Gly | Phe | Lys | Met 335 | His |
| 35 | Ala | Arg | Gly | Trp 340 | Ile | Ser | Ile | Tyr | Cys 345 | Asn | Pro | Pro | Arg | Pro 350 | Ala | Phe |
| | Lys | Gly | Ser 355 | Ala | Pro | Ile | Asn | Leu 360 | Ser | Asp | Arg | Leu | Asn 365 | Gln | Val | Lev |

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| | Arg | Trp 370 | Ala | Leu | Gly | Ser | Ile 375 | Glu | Ile | Leu | Leu | Ser 380 | Arg | His | Cys | Pro |
|----|-----|------------|------------|------------|------------|-----|-------------|------------|-----|-------|-----|------------|------------|------------|-----|-----|
| | *1- | | | 61 | | ••• | ~ 1. | | • | S | • | _ | | | | |
| 5 | 385 | Trp | Tyr | GIY | Tyr | 390 | GIY | Arg | Leu | Arg | 395 | Leu | Glu | Arg | Ile | A1a |
| | Tyr | Ile | Asn | Thr | Ile | Val | Tyr | Pro | Ile | Thr | Ser | Ile | Pro | Leu | Ile | Ala |
| | | | | | 405 | | - | | | 410 | | | | | 415 | |
| 10 | туг | Сув | Ile | Leu | Pro | Ala | Phe | Сув | Leu | Ile | Thr | qaA | Arg | Phe | Ile | Ile |
| | | | | 420 | | | | | 425 | | | | | 430 | | |
| | Pro | Glu | Ile 435 | Ser | Asn | Tyr | Ala | Ser | Ile | Trp | Phe | Ile | Leu 445 | Leu | Phe | Ιlε |
| 15 | | | | | | | | | | | | | | | | |
| | Ser | Ile 450 | Ala | Val | Thr | Gly | Ile 455 | Leu | Lys | Leu | Lys | Trp 460 | Asn | Gly | Val | Ser |
| | Ile | Glu | Asp | Trp | Trp | Arg | Asn | Asn | Gln | Phe | Trp | Val | Ile | Gly | Gly | Thr |
| 20 | 465 | | | | | 470 | | | | | 475 | | | | | 480 |
| | Ser | Thr | His | Leu | Phe | Ala | Val | Phe | Gln | Gly | Leu | Leu | Lys | Val | Leu | Ala |
| | | | | | 485 | | | | | 490 | | | | | 495 | |
| 25 | Gly | Ile | Asn | Thr 500 | Asn | Phe | Thr | Val | Thr | Ser | Lys | Ala | Thr | Asn 510 | Lys | Asr |
| | | | | | | | | | | | | | | | | |
| | Gly | Asp | Phe 515 | Ala | Lys | Leu | Tyr | 11e 520 | Phe | Lys | Trp | Thr | Ala 525 | Leu | Leu | Ile |
| 30 | Pro | Pro | Thr | Thr | Val | Leu | Leu | Val | Asn | Leu | Ile | Gly | Ile | Val | Ala | Glv |
| | | 530 | | | | | 535 | | | | | 540 | | | | • |
| | Val | Ser | Туr | Ala | Val | Asn | Ser | Gly | туг | Gln | Ser | Trp | Gly | Pro | Leu | Phe |
| 35 | 545 | | | | | 550 | | | | | 555 | | | | | 560 |
| | Gly | Lys | Leu | Phe | Phe 565 | Ala | Leu | Trp | Val | Ile | Ala | His | Leu | Tyr | Pro | Phe |
| | | | | | 202 | | | | | 2 / V | | | | | 3/5 | |

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Leu Lys Gly Leu Leu Gly Arg Gln Asn Arg Thr Pro Thr Ile Val Ile 580 585 590

Val Trp Ser Val Leu Leu Ala Ser Ile Phe Ser Leu Leu Trp Val Arg 5 595 600 605

Ile Asn Pro Phe Val Asp Ala Asn Pro Asn Ala Asn Asn Phe Asn Gly
610 615 620

10~Lys Gly Gly Val Phe 625

- 94 -

```
(2) INFORMATION FOR SEQ ID NO:3:
```

(i) SEQUENCE CHARACTERISTICS:

5 (A) LENGTH: 8411 base pairs

(B) TYPE: nucleic acid(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

10 (ii) MOLECULE TYPE: DNA (genomic)

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

15

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Arabidopsis thaliana

(B) STRAIN: Columbia (wild-type)

20 (vii) IMMEDIATE SOURCE:

(B) CLONE: 23H12 RSW1 GENE

(ix) FEATURE:

25 (A) NAME/KEY: exon

(B) LOCATION: 2296..2376

(ix) FEATURE:

(A) NAME/KEY: exon

30 (B) LOCATION: 2904..3099

(ix) FEATURE:

(A) NAME/KEY: exon

(B) LOCATION: 3198..3370

35

(ix) FEATURE:

(A) NAME/KEY: exon

(B) LOCATION: 3594..3708

40 (ix) FEATURE:

- 95 -

(A) NAME/KEY: exon (B) LOCATION: 3824..4013 (ix) FEATURE: 5 (A) NAME/KEY: exon (B) LOCATION: 4181..4447 (1x) FEATURE: (A) NAME/KEY: exon 10 (B) LOCATION: 4783..5128 (1x) FEATURE: (A) NAME/KEY: exon (B) LOCATION: 5207..5344 15 (ix) FEATURE: (A) NAME/KEY: exon (B) LOCATION: 5426..5551 20 (ix) FEATURE: (A) NAME/KEY: exon (B) LOCATION: 5703..5915 (ix) FEATURE: 25 (A) NAME/KEY: exon (B) LOCATION: 6022..6286 (ix) FEATURE: (A) NAME/KEY: exon 30 (B) LOCATION: 6374..6570 (ix) FEATURE:

(A) NAME/KEY: exon

(B) LOCATION: 6655..7005

35

(ix) FEATURE:

(A) NAME/KEY: exon

(B) LOCATION: 7088..8032

40

- 96 -

(x1) SEQUENCE DESCRIPTION: SEQ ID NO:3:

40

| | TTAGAAGAAG | CCTGAGCCGG | AGTCCTATTC | AATTATCTAG | AAGAAGTCTG | AGCCGGAGTC | 60 |
|----|------------|------------|------------|------------|------------|------------|------|
| 5 | CCACTCGATT | GTCTAGGAGA | AGCCTAAGCC | GGAGTCCCAT | TCGATCACCT | AGGAAGAGTG | 120 |
| | TGAGCAGGAG | TCCAGTCCGA | TCATCTAGGA | AGAGTGTGAG | CAGAAGTCCG | GTTCGTTCAT | 180 |
| 10 | CCAGGAGACG | TATCAGCAGG | AGTCCAGTCC | GATCATCTAG | GAAGAGTGTG | AGCAGGAGTC | 240 |
| | CTATTCGATT | GTCCAGAAGA | AGTATCAGCA | GGAGTCCTAT | TCGATTGTCC | AGGAGAAGTA | 300 |
| | TCAGCAGGAG | TCCTGTTAGA | GGAAGAAGAA | GAATTAGCAG | AAGTCCAGTT | CCGGCAAGGA | 360 |
| 15 | GAAGGAGTGT | GCGGCCTAGA | тстсстсстс | CTGACCGCAG | AAGAAGTTTG | TCAAGAAGTG | 420 |
| | CTTCTCCTAA | TGGGCGCATA | AGGAGAGGGA | GAGGATTTAG | CCAAAGATTC | TCATACGCCC | 480 |
| 20 | GTCGATACAG | AACTAGTCCA | TCTCCTGATC | GATCTCCTTA | TCGCTTTAGT | GATAGGAGTG | 540 |
| | ACCGTGACAG | GTGAATAGCC | CACACATAAT | ATAACTCCCC | CTTTCTGTTA | CACACTCTCG | 600 |
| | TACTGAACCG | TCTTTTTAT | AACGTCTTCT | CTGTAGATTT | AGAAGTCGCA | GAAGGTTCTC | 660 |
| 25 | GCCAAGTCGG | TTCAGAAGCC | CACTAAGAGG | AAGAACACCT | CCAAGGTACT | TATCCTCTTT | 720 |
| | AGTACATTGT | TTCAGCTGAT | TCTTTACATC | TAAAAGTTTC | ATGAATATGG | AACTAAAATT | 780 |
| 30 | GGTGATCCAA | AAGAATTATT | CTTGATTTCA | CAACTCGAAA | GTATGCTCAG | GTATAGAAGA | 840 |
| | AGAAGCCGCT | CAGTATCGCC | TGGTCTCTGT | TATCGCAACC | GGCGGTACAG | CCGCAGCCCT | 900 |
| | ATCCGTAGCC | GATCTCCACC | TTACAGAAAG | AGAAGGTCAC | CATCCGCTAG | CCACAGCCTG | 960 |
| 35 | AGTCCATCGA | GGTCAAGATC | AAGATCAAAG | TCATATTCAA | AATCTCCCAT | TGGGACGGGG | 1020 |
| | AAAGCAAGAT | CAGTGTCAAG | ATCACCATCC | AAGGCAAGGT | CTCCATCGAA | GTCGGATTCG | 1080 |
| | ACATCCTCGG | ATAATAGCCC | AGGTGGGAAA | AAGGGATTAG | TAGCCTATGA | TTAATGAATA | 1140 |

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| | | ATGATTACCC | TTAAGTTAAG | TGTTTGTTCT | TTTTACTGAG | AAGAGATGGT | AAAGAGAGTA | 1200 |
|---|----|------------|------------|------------|------------|------------|------------|------|
| | | AGTAGTTTAC | TTCTGTAAAA | CATAAGCATT | GTCTTTTGCG | TATGTTTGTT | TGATTATGCT | 1260 |
| | 5 | CCAAGATTGT | TAAAAATTTC | TGTTGATGTT | TGCCGACATT | TTTTCTTTGT | TGCCATTTGC | 1320 |
| | | CGACAAATGT | TAACTTCCAT | TATTCGTTGC | GGAGTTGGTT | TTGGTCCAAT | AATTAAACTT | 1380 |
| | 10 | TCATAAAATT | AAGCATAACT | AAATGTGACG | TTTGTCACCA | AACTTTAGAA | CAACGACATC | 1440 |
| | | GTAATTTATT | TATTTGGATA | ATCAATATAA | TTTACGATTT | CTTCCTACAT | АТАТАТСАТА | 1500 |
| | | TCACTATACC | ACCGTCATTA | TCACTATCAC | TAAATATAAA | AATGTTAAAA | TGATTTCTTA | 1560 |
| | 15 | ATGGAATTTT | TTTTGTTAAA | AGTTTATTGA | CACAAAAAAT | GAATTAAAAC | TCAGAAATCT | 1620 |
| | | GTATACTGAA | TTAAAACTTG | TAAATATAAC | AACAAAATGG | GATTAAAAAA | AGAAGTGGCA | 1680 |
| | 20 | TCCATTTAAA | AATTATTTGC | GAATTCGCCC | GTAACTTCTT | AAGCTAACAA | TTAGAACCTA | 1740 |
| • | 20 | ATCAACACTA | GTTATTTGA | GTCCACCGAC | AGGTGATAGC | AAATAAAA | GAACAGGCTG | 1800 |
| | | GTACCAGAGC | CAACAACAAC | GTGGCTTCTT | CTTTTTTTT | ТТТААТАТАА | TCAAACAATC | 1860 |
| : | 25 | ATACTTTGTC | CTATCTCTTT | CTTGCAATAA | GATTTTGCCA | CGTCACATAC | TAAGAAGCTG | 1920 |
| | | GCGCGTCTAG | TGGGGAAGCC | AGAACGGCTC | ACTTTAAAAA | GTAGAGAGAT | GATAACTTGA | 1980 |
| | 30 | GCCGAATAGA | GCCGAGCTGA | GCTAAAACGG | TGGGAGAGGA | AGAGGCTACT | ACTACCGTCA | 2040 |
| | | CCATCTCCGG | TAAAATAATG | TACTTGTCAT | TTAAAAATTA | AGAAAAAACA | CATCACTCTG | 2100 |
| | | CGATAAAATA | GGCAAAAGCA | GATTTGAAGA | AGAAGCAGCT | TGAGATATCA | AATAGAGAGA | 2160 |
| | 35 | GAGAGTGACA | GAGGAGTGTG | TGAACATCCT | TTTTTAGTAG | ATTTGGGTTT | TCGAGATGCC | 2220 |
| | | GTATTGAATC | GGCTACGAAT | TTCCCAATTT | TGAATTTTGT | GAATCTCTCT | CTTTCTCTGT | 2280 |
| | 40 | GTGTCGGTGG | CTGCGATGGA | GGCCAGTGCC | GGCTTGGTTG | CTGGATCCTA | CCGGAGAAAC | 2340 |
| | | | | | | | | |

| | GAGCTCGTTC | GGATCCGACA | TGAATCTGAT | GGCGGGGTCT | GTTCATCTTC | CCTTTTTCCC | 2400 |
|----|------------|------------|------------|------------|------------|------------|------|
| | ATTTTTTTGT | TATTGTTTTT | CGTTCTTACA | ATTTTTGATG | TGTAGATCTC | ATCTAGATTT | 2460 |
| 5 | СТСТСТТТСТ | AAATCTCGTC | TCTTTTGGAT | CCATAATTGG | ATCATTGAAA | CTCAGATTTC | 2520 |
| | GCTTCCTTTG | ACTGTGTAGT | TAGTTAGTGT | CAGTTGATCA | AGTAAGTGTC | TGAAAATGGA | 2580 |
| 10 | AACTTTTCTG | CTCCAATTCT | TCAAATTGTT | GTGATCTATA | TCAATTAATG | CCGCATCTGT | 2640 |
| 10 | тттсттаааа | TCTCTTATGG | AAAGTGTCGG | TGGATTTCAG | TTCGTTAACT | TTTTTAAGCT | 2700 |
| | AAAATCTTTG | ACTCTTAAAG | TTTAGCTTTA | CTTATTGAGA | TTTAGCTCAA | CTAGATCTCG | 2760 |
| 15 | TTAGTTCCCG | CCATGGGATA | CAGACTGTGA | CTCGCCTTAA | TTCAGATCTG | CATTGATTGT | 2820 |
| | TTTGATTTAG | ATCCTTGCTC | ATCTCTTTCT | GTAGTTTCTA | ATACTCAATG | ACTAACAATG | 2880 |
| 20 | ATGCAATGTT | GGTCAAAGTG | CAGACCAAAC | CTTTGAAGAA | TATGAATGGC | CAGATATGTC | 2940 |
| 20 | AGATCTGTGG | TGATGATGTT | GGACTCGCTG | AAACTGGAGA | TGTCTTTGTC | GCGTGTAATG | 3000 |
| | AATGTGCCTT | CCCTGTGTGT | CGGCCTTGCT | ATGAGTACGA | GAGGAAAGAT | GGAACTCAGT | 3060 |
| 25 | GTTGCCCTCA | ATGCAAGACT | AGATTCAGAC | GACACAGGGG | TCAGTTGTCT | ттттсттттт | 3120 |
| | GTTGGCAATT | GCTATATATG | GATTTTCTCT | TTTTGTTTCT | TTGCTGTTGT | GTTGAACAAT | 3180 |
| 30 | TTTTTGGAAT | TTTCCAGGGA | GTCCTCGTGT | TGAAGGAGAT | GAAGATGAGG | ATGATGTTGA | 3240 |
| 30 | TGATATCGAG | AATGAGTTCA | ATTACGCCCA | GGGAGCTAAC | AAGGCGAGAC | ACCAACGCCA | 3300 |
| | TGGCGAAGAG | TTTTCTTCTT | CCTCTAGACA | TGAATCTCAA | CCAATTCCTC | TTCTCACCCA | 3360 |
| 35 | TGGCCATACG | GTAGGGACCT | ACATTTTCCC | TTTAGACTCT | AGAGTGATTT | GTATTACTCA | 3420 |
| | ATAAATCCCT | AGAGTGGTCA | TTTATTACTT | ACTATTCACG | TTAATGTTAT | ATGTGAACAA | 3480 |
| 40 | ATCTTAACAG | AATTTTTTC | TGATAGTACA | TGGTCATCCA | AATTAAGAAA | TAATAATAGA | 3540 |
| | | | | | | | |

| | TGTTGTTAGT | TGTGTCTGTT | TTCAATAGAT | TCATGACCTT | TTTCTATACA | CAGGTTTCTG | 3600 |
|----|------------|------------|------------|------------|------------|------------|------|
| | GAGAGATTCG | CACGCCTGAT | ACACAATCTG | TGCGAACTAC | ATCAGGTCCT | TTGGGTCCTT | 3660 |
| 5 | CTGACAGGAA | TGCTATTTCA | TCTCCATATA | TTGATCCACG | GCAACCTGGT | ATTCATATGT | 3720 |
| | TTTTCCCTTG | TGCACGTGGT | CTTTGTTAAA | TGTGATTCCT | ATTCATTTT | ACAACATATA | 3780 |
| 10 | TATTTTGTGT | ACCGTAACTG | ATAGCTCCCG | CTAAAAATTG | CAGTCCCTGT | AAGAATCGTG | 3840 |
| •• | GACCCGTCAA | AAGACTTGAA | CTCTTATGGG | CTTGGTAATG | TTGACTGGAA | AGAAAGAGTT | 3900 |
| | GAAGGCTGGA | AGCTGAAGCA | GGAGAAAAT | ATGTTACAGA | TGACTGGTAA | ATACCATGAA | 3960 |
| 15 | GGGAAAGGAG | GAGAAATTGA | AGGGACTGGT | TCCAATGGCG | AAGAACTCCA | AATGTAAGTG | 4020 |
| | GAAATACTAG | ACCAATATCT | TTATTGTCCA | ACTCAAACAG | CTCTTGGCCG | TGATGCTAAT | 4080 |
| 20 | AACCACTCTT | GGTTTCTTAT | TATGTATTGA | TAGACATAAT | TAAGTATCTG | CTTTGTTACA | 4140 |
| | TTTGTTTCCT | TCCACTCAAT | TATGGTTCTC | GTACTTACAG | GGCTGATGAT | ACACGTCTTC | 4200 |
| | CTATGAGTCG | TGTGGTGCCT | ATCCCATCTT | CTCGCCTAAC | CCCTTATCGG | GTTGTGATTA | 4260 |
| 25 | TTCTCCGGCT | TATCATCTTG | TGTTTCTTCT | TGCAATATCG | TACAACTCAC | CCTGTGAAAA | 4320 |
| | ATGCATATCC | TTTGTGGTTG | ACCTCGGTTA | TCTGTGAGAT | CTGGTTTGCA | TTTTCTTGGC | 4380 |
| 30 | TTCTTGATCA | GTTTCCCAAA | TGGTACCCCA | TTAACAGGGA | GACTTATCTT | GACCGTCTCG | 4440 |
| | CTATAAGGTT | GGTCTTTAAG | TTTATACATC | CCCTACTCTC | ATCTCTCTTT | TATGTATTAA | 4500 |
| | CTTGATATCT | TCTATCACAG | TTTTCGATAG | TTGACTTTTT | CCCCTGTAA | ATTTAATTTA | 4560 |
| 35 | AATTTAGACA | ATGGTGCATC | TGAATTTTGA | TTATGATATA | TCTTAAGAAG | ATTATGATTG | 4620 |
| | TAAATCTTGA | AATTTAGTAG | AAAACCATCT | GCAATCTACT | GACCATGTGA | AGTTTCCGAC | 4680 |
| 40 | TAGACTATGA | TAGAAGCATG | CCAAGTGGAG | TGTTTATTAA | GATAGAGCTT | AGCTATTATA | 4740 |

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| | CTGATTTTAT | ATGTGTTTTG | ATTTTTTGGT | TTCTTATTGT | AGATATGATC | GAGACGGTGA | 4800 |
|----|------------|------------|------------|------------|------------|------------|------|
| | ACCATCACAG | CTCGTTCCTG | TTGATGTGTT | TGTTAGTACA | GTGGACCCAT | TGAAAGAGCC | 4860 |
| 5 | тссссттстт | ACAGCAAACA | CAGTTCTCTC | GATTCTTTCT | GTGGACTACC | CGGTAGATAA | 4920 |
| | AGTAGCCTGT | TATGTTTCAG | ATGATGGTTC | AGCTATGCTT | ACCTTTGAAT | CCCTTTCTGA | 4980 |
| 10 | AACCGCTGAG | TTTGCAAAGA | AATGGGTACC | ATTTTGCAAG | AAATTCAACA | TTGAACCTAG | 5040 |
| | GGCCCCTGAA | TTCTATTTTG | CCCAGAAGAT | AGATTACTTG | AAGGACAAGA | TCCAACCGTC | 5100 |
| | TTTTGTTAAA | GAGCGACGAG | CTATGAAGGT | CATTTGAAAA | GTCCACCTGC | TTCTCATCCA | 5160 |
| 15 | TACGGCAAAG | AGATTGACTG | ACTTTTTCTT | TGGTTTGTAT | TGACAGAGAG | AGTATGAAGA | 5220 |
| | GTTTAAAGTG | AGGATAAATG | CTCTTGTTGC | CAAAGCACAG | AAAATCCCTG | AAGAAGGCTG | 5280 |
| 20 | GACAATGCAG | GATGGTACTC | CCTGGCCTGG | TAACAACACT | AGAGATCATC | CTGGAATGAT | 5340 |
| | ACAGGTACAG | TGTGGCAATC | CCTTGATTGT | GACAGAGAGG | ATAACGTAAA | GGAAACATGT | 5400 |
| | TTACATCGTT | TTGTTTCAAT | TTCAGGTGTT | CTTAGGCCAT | AGTGGGGGTC | TGGATACCGA | 5460 |
| 25 | TGGAAATGAG | CTGCCTAGAC | TCATCTATGT | TTCTCGTGAA | AAGCGGCCTG | GATTTCAACA | 5520 |
| | CCACAAAAAG | GCTGGAGCTA | TGAATGCATT | GGTTTGTTAA | CTTTCAGAAT | CCTATTGTGT | 5580 |
| 30 | CCTCTATTTT | ATTCTCTTGT | TCACTGCCTA | AGAAACGTTC | TTCTTGTGTA | GCCGTTGCTT | 5640 |
| | CACATTCTTT | TTTTTCTAGG | CTATGTGTTC | TCTCCTAATT | TAGTATCTCT | TTACTTTGAC | 5700 |
| | AGATCCGTGT | ATCTGCTGTT | CTTACCAATG | GAGCATATCT | TTTGAACGTG | GATTGTGATC | 5760 |
| 35 | ATTACTTTAA | TAACAGTAAG | GCTATTAAAG | AAGCTATGTG | TTTCATGATG | GACCCGGCTA | 5820 |
| | TTGGAAAGAA | GTGCTGCTAT | GTCCAGTTCC | CTCAACGTTT | TGACGGTATT | GATTTGCACG | 5880 |
| 40 | ATCGATATGC | CAACAGGAAT | ATAGTCTTTT | TCGATGTGAG | TATCACTTCC | CCATTGTCTT | 5940 |

| | TTGTTTCTCT | TTTGTTCATA | TTTTGGTTGG | ATTTACTCGT | TTCTGCTATG | GCCTGACTTG | 6000 |
|----|------------|------------|------------|------------|------------|------------|------|
| | GATATTTGTT | CTCTTGGGCA | GATTAACATG | AAGGGGTTGG | ATGGTATCCA | GGGTCCAGTA | 6060 |
| 5 | TATGTGGGTA | CTGGTTGTTG | TTTTAATAGG | CAGGCTCTAT | ATGGGTATGA | TCCTGTTTTG | 6120 |
| | ACGGAAGAAG | ATTTAGAACC | TTATTATAAA | GTCAAGAGCT | GTTGCGGGTC | AAGGAAGAAA | 6180 |
| 10 | GGTAAAAGTA | GCAAGAAGTA | TAACTACGAA | AAGAGGAGAG | GCATCAACAG | AAGTGACTCC | 6240 |
| | AATGCTCCAC | TTTTCAATAT | GGAGGACATC | GATGAGGGTT | TTGAAGGTTT | GATTGAGCTG | 6300 |
| | ATTGTGTAAT | AACATCACTT | CTTTATGTAA | TGATTTATGT | GATGGTGAAA | TCTTACAATC | 6360 |
| 15 | CTTGTTTATG | CAGGTTATGA | TGATGAGAGG | тстаттстаа | TGTCCCAGAG | GAGTGTAGAG | 6420 |
| | AAGCGTTTTG | GTCAGTCGCC | GGTATTTATT | GCGGCAACCT | TCATGGAACA | AGGCGGCATT | 6480 |
| 20 | CCACCAACAA | CCAATCCCGC | TACTCTTCTG | AAGGAGGCTA | TTCATGTTAT | AAGCTGTGGT | 6540 |
| 20 | TACGAAGACA | AGACTGAATG | GGGCAAAGAG | GTCAGTTTTC | AAATGCAGCT | ACAGAATCTT | 6600 |
| | CTTATGTTCT | CTTTCTTACC | TGTTTGATGA | CATCTTATTT | GGCACTTTTG | TTAGATTGGT | 6660 |
| 25 | TGGATCTATG | GTTCCGTGAC | GGAAGATATT | CTTACTGGGT | TCAAGATGCA | TGCCCGGGGT | 6720 |
| | TGGATATCGA | TCTACTGCAA | TCCTCCACGC | CCTGCGTTCA | AGGGATCTGC | ACCAATCAAT | 6780 |
| 30 | CTTTCTGATC | GTTTGAACCA | AGTTCTTCGA | TGGGCTTTGG | GATCTATCGA | GATTCTTCTT | 6840 |
| 50 | AGCAGACATT | GTCCTATCTG | GTATGGTTAC | CATGGAAGGT | TGAGACTTTT | GGAGAGGATC | 6900 |
| | GCTTATATCA | ACACCATCGT | CTATCCTATT | ACATCCATCC | CTCTTATTGC | GTATTGTATT | 6960 |
| 35 | CTTCCCGCTT | TTTGTCTCAT | CACCGACAGA | TTCATCATAC | CCGAGGTTTG | TAAAACTGAC | 7020 |
| | CACACTGCTA | TTTACTATTT | GAATCCCATT | TTGTGAATGC | ATTTTTTGT | CATCATCATT | 7080 |
| 40 | GTTGCAGATA | AGCAACTACG | CGAGTATTTG | GTTCATTCTA | CTCTTCATCT | CAATTGCTGT | 7140 |
| | | | | | | | |

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| | GACTGGAATC | CTGGAGCTGA | GATGGAGCGG | TGTGAGCATT | GAGGATTGGT | GGAGGAACGA | 7200 |
|----|------------|------------|------------|------------|------------|------------|------|
| | GCAGTTCTGG | GTCATTGGTG | GCACATCCGC | CCATCTTTTT | GCTGTCTTCC | AAGGTCTACT | 7260 |
| 5 | TAAGGTTCTT | GCTGGTATCG | ACACCAACTT | CACCGTTACA | TCTAAAGCCA | CAGACGAAGA | 7320 |
| | TGGGGATTTT | GCAGAACTCT | ACATCTTCAA | ATGGACAGCT | CTTCTCATTC | CACCAACCAC | 7380 |
| 10 | CGTCCTACTT | GTGAACCTCA | TAGGCATTGT | GGCTGGTGTC | TCTTATGCTG | TAAACAGTGG | 7440 |
| | CTACCAGTCG | TGGGGTCCGC | TTTTCGGGAA | GCTCTTCTTC | GCCTTATGGG | TTATTGCCCA | 7500 |
| | TCTCTACCCT | TTCTTGAAAG | GTCTGTTGGG | AAGACAAAAC | CGAACACCAA | CCATCGTCAT | 7560 |
| 15 | TGTCTGGTCT | GTTCTTCTCG | CCTCCATCTT | CTCGTTGCTT | TGGGTCAGGA | TCAATCCCTT | 7620 |
| | TGTGGACGCC | AATCCCAATG | CCAACAACTT | CAATGGCAAA | GGAGGTGTCT | TTTAGACCCT | 7680 |
| 20 | ATTTATATAC | TTGTGTGTGC | АТАТАТСААА | AACGCGCAAT | GGGAATTCCA | AATCATCTAA | 7740 |
| 20 | ACCCATCAAA | CCCCAGTGAA | CCGGGCAGTT | AAGGTGATTC | CATGTCCAAG | ATTAGCTTTC | 7800 |
| | TCCGAGTAGC | CAGAGAAGGT | GAAATTGTTC | GTAACACTAT | TGTAATGATT | TTCCAGTGGG | 7860 |
| 25 | GAAGAAGATG | TGGACCCAAA | TGATACATAG | TCTACAAAAA | GAATTTGTTA | TTCTTTCTTA | 7920 |
| | TATTTATTTT | ATTTAAAGCT | TGTTAGACTC | ACACTTATGT | AATGTTGGAA | CTTGTTGTCC | 7980 |
| 30 | TAAAAAGGGA | TTGGAGTTTT | СТТТТТАТСТ | AAGAATCTGA | AGTTTATATG | CTAAGCTTTT | 8040 |
| | CACTTTACTA | CAAAAAGTTT | ATGGATATGA | TGGTGTACGT | CAATTGTTGG | TGCAAGTGTT | 8100 |
| | GATGTCTTCG | GGTGAACTCG | CCCTCTTGTT | TTGTCTCACC | CATCAGTACA | AATAGAATGA | 8160 |
| 35 | CATTTATTTT | TTTGAACTTT | TAACGAAATC | TTTGTCATTA | TGGGACTTGA | TCAGTAAAGT | 8220 |
| | TACATATTTG | AAGAGATATT | GTGTAAACTC | TTATTTGAAT | CAGAATCAGA | TCAATCAAAA | 8280 |
| 40 | ATTGAAAACG | TAAAGTTCAA | ACAAAAAGGT | AGAGTGAATC | TTTTAATCCC | CCCTCAATAC | 8340 |
| | | | | | | | |

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8400 TAATTTGTGA AATCTCAAGT GGTGTAAAAT GAACCCAATT AGTATCCACA ATGTGTTTCT 8411 CTGATCAATC C 5 (2) INFORMATION FOR SEQ ID NO:4: (i) SEQUENCE CHARACTERISTICS: 10 (A) LENGTH: 5009 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear 15 (ii) MOLECULE TYPE: DNA (genomic) (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 20 (vi) ORIGINAL SOURCE: (A) ORGANISM: Arabidopsis thaliana (B) STRAIN: Columbia 25 (vii) IMMEDIATE SOURCE: (B) CLONE: 12C4 (ix) FEATURE: (A) NAME/KEY: exon 30 (B) LOCATION: 863..943 (ix) FEATURE: (A) NAME/KEY: exon (B) LOCATION: 1454..1840 35 (ix) FEATURE: (A) NAME/KEY: exon (B) LOCATION: 1923..2025

40

(ix) FEATURE:

- 104 -

(A) NAME/KEY: exon

(B) LOCATION: 2122..2311

| | (ix) | FEAT | URE: | | | | | |
|----|----------|-------|------------|------------|------------|------------|------------|-----|
| 5 | | (A) | NAME/KEY: | exon | | | | |
| | | (B) | LOCATION: | 2421268 | 7 | | | |
| | (ix) | FEAT | URE: | | | | | |
| | | (A) | NAME/KEY: | exon | | | | |
| 10 | | (B) | LOCATION: | 2776312 | 1 | | | |
| | (ix) | FEAT | URE: | | | | | |
| | | (A) | NAME/KEY: | exon | | | | |
| | | (B) | LOCATION: | 3220335 | 7 | | | |
| 15 | | | | | | | | |
| | (ix) | FEAT | | | | | | |
| | | | NAME/KEY: | | - | | | |
| | | (8) | LOCATION: | 3507362 | 3 | | | |
| 20 | (ix) | FEAT | URE: | | | | | |
| | | (A) | NAME/KEY: | exon | | | | |
| | | (B) | LOCATION: | 3723393 | 5 | | | |
| | (ix) | FEAT | URE: | | | | | |
| 25 | | (A) | NAME/KEY: | exon | | | | |
| | | (B) | LOCATION: | 4027429 | 7 | | | |
| | (ix) | FEAT | URE: | | | | | |
| | | (A) | NAME/KEY: | exon | | | | |
| 30 | | (B) | LOCATION: | 4380457 | 6 | | | |
| | | | | | | | | |
| | (xi) | SEQU | ENCE DESCR | IPTION: SE | Q ID NO:4: | | | |
| 35 | AAGGAATA | ат аа | GATAGGGG T | TTAATGGGA | GACAATCAAT | CTTCAGGGGT | TTTCTGGAAN | 60 |
| | AACGGCGG | GG TA | AAAAACAA G | ACATCAATC | GGACCCGATC | ACGAGGACCC | GGATCCGNAT | 120 |
| 40 | CGATAAAC | AG NG | TAGCTTTC A | ATACCCCAT | TTTCCCAGAA | ACACCTCTCA | AAAATTTTTT | 180 |
| 70 | | | | | | | | |

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| | CAAGAACTNG | TATAAATATC | TCAGTTTCGT | TCACGCAGGT | CTTTNTTATT | TTGGNAANTC | 240 |
|----|------------|------------|------------|------------|------------|------------|------|
| | TNTNTTCATN | GTTCACCAAC | TCCCTCTTGA | AGGTGGGACA | GAGTCCAGCT | CCACCACCAC | 300 |
| 5 | CATAGCCATC | GCGTCGTTTT | CTCCGGGACC | CACTTATTTC | GTGACGTTTC | TCTCTTTGTA | 360 |
| | TATACATACA | ATTGTTTTCA | GTCTCAATTT | GCTGTCCACA | TTTTAACACA | ACTCTATCTC | 420 |
| 10 | AGGGGTGGTG | TCTGAATCTC | GTCTCTCTCA | TTCCTATTTA | TCCCAATCTA | ATCTATCACA | 480 |
| | AACCCTTCCA | CATTGCTTTT | GTCAGTCTGT | AAAATTCTCT | TTGAATCAGT | GAATCACTCA | 540 |
| | CTTAAATCCA | AAACAGTTTT | TTTTTCTTTC | TTTCTTTATT | TGCTTGTTGT | GGAATCAATA | 600 |
| 15 | GCTGTCTCCG | GGAAAATTCG | ТТТТТТТТСТ | CCTTCGGGAT | CTCTTTTTT | TTTTTTTGG | 660 |
| | TTTTATTTAA | TAATTATCCC | CGAGCCAACA | TTTATTGTCG | ATTCGGTTTA | TTTCGTCTCC | 720 |
| 20 | TTCGTCTTCC | ACTCTTACTA | GTGCATGCTC | TGAATCTGTA | TGTAATGGGA | GTTCAACAGT | 780 |
| 20 | CTGGATCCAT | TATCCTAGCC | GGGTCGGGTC | AAGGTCTTTG | AGTAAGAGAG | ACAATTCGTT | 840 |
| | TTGATTCGGT | GTAGAAGACA | TCATGAATAC | TGGTGGTCGG | CTCATTGCTG | GCTCTCACAA | 900 |
| 25 | CAGAAACGAA | TTCGTTCTCA | TTAACGCCGA | TGAGAGTGCC | AGAGTAAGAA | TAACTTTTGT | 960 |
| | ANGAATTTGT | GACGGAAAAA | AGTTTAATTT | TTTCTCTTTC | TTGGGGATCT | AGATTATGAG | 1020 |
| 30 | AATCTAGATG | GAATATTTTG | ATCTGAAATT | GGAAGTTTCT | AGGGAGTAAT | GCCGCAACCC | 1080 |
| | ACATGTTCTG | TTTTTTCTTT | TTTCTTTCT | TCAAGTAGTG | TTGCATGATT | CATACGTGTC | 1140 |
| | GGCAGAGATG | TCCTGAGAAC | CGAATTCAAT | GTTGTAGCAG | TAGCAATAAG | TTCAAAGAAA | 1200 |
| 35 | GTCCATTTT | TTATATTACT | AATTCTGTTC | TTGGTTTATT | TGAGCTGGTC | TTTATTGCAT | 1260 |
| | TTCACCTGGA | TTCAGATACT | AATAACTGTC | TCAATTATGT | AAAAATGACA | ACTTTATGAA | 1320 |
| 40 | ATTCAGTTTC | ACAATTATGT | AATTCATAAT | CGATGAATGT | TTTTCTTGAG | TCTTTATCAT | 1380 |
| _ | | | | | | | |

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| | CTTTAGGATT | TGATTAAGAT | GCAATTTGAT | GAAAATACTA | AAAAGACTCA | TGTGTTCTCA | 1440 |
|----|------------|------------|------------|------------|------------|------------|------|
| | TTTCTCTATG | TAGATACGAT | CAGTACAAGA | ACTGAGTGGG | CAAACATGTC | AAATCTGTGG | 1500 |
| 5 | AGATGAAATC | GAATTAACGG | TTAGCAGTGA | GCTCTTTGTT | GCTTGCAACG | AATGCGCATT | 1560 |
| | CCCGGTTTGT | AGACCATGCT | ATGAGTATGA | ACGTAGAGAA | GGAAATCAAG | CTTGTCCTCA | 1620 |
| 10 | GTGCAAAACT | CGATACAAAA | GGATTAAAGG | TAGTCCACGG | GTTGATGGAG | ATGATGAAGA | 1680 |
| 10 | AGAAGAAGAC | ATTGATGATC | TTGAGTATGA | GTTTGATCAT | GGGATGGACC | CTGAACATGC | 1740 |
| | CGCTGAAGCC | GCACTCTCTT | CACGCCTTAA | CACCGGTCGT | GGTGGATTGG | ATTCAGCTCC | 1800 |
| 15 | ACCTGGCTCT | CAGATTCCTC | TTTTGACTTA | TTGTGATGAA | GTGAGGAATC | CAAATTGTTT | 1860 |
| | GTTTTCTCTG | ACAATGTTGT | TGCTTAGATG | ATTCTTTTTC | TTATTAGTCT | ATGTGTTTTC | 1920 |
| 20 | AGGATGCTGA | TATGTATTCT | GATCGTCATG | CTCTTATCGT | GCCTCCTTCA | ACGGGATATG | 1980 |
| | GGAATCGCGT | CTATCCTGCA | CCGTTTACAG | ATTCTTCTGC | ACCTCGTATG | TGTTTACTTT | 2040 |
| | TATGATTCCT | ACAATTTTTC | TTCTTATATG | ATTTGGTCAC | CTTCTAATGA | GTTATGAAAT | 2100 |
| 25 | GGTTTTGTTT | GTTGTTTTCA | GCACAGGCGA | GATCAATGGT | TCCTCAGAAA | GATATTGCGG | 2160 |
| | AATATGGTTA | TGGAAGTGTT | GCTTGGAAGG | ACCGTATGGA | AGTTTGGAAG | AGACGACAAG | 2220 |
| 30 | GCGAAAAGCT | TCAAGTCATT | AAGCATGAAG | GAGGAAACAA | TGGTCGAGGT | TCCAATGATG | 2280 |
| | ACGACGAACT | AGATGATCCT | GACATGCCTA | TGTAAGTTGT | таааатстаа | CAAAAGTTCA | 2340 |
| | GATGAAATGA | TGCTCTGAAA | TTTTGTGTTC | AATGGNTTTG | TTTTCTTATT | GTTGTTTAAA | 2400 |
| 35 | CATTTTTCGT | GCTAATTCAG | GATGGATGAA | GGAAGACAAC | CTCTCTCAAG | AAAGCTACCT | 2460 |
| | ATTCGTTCAA | GCAGAATAAA | TCCTTACAGG | ATGTTAATTC | TGTGTCGCCT | CGCGATTCTT | 2520 |
| 40 | | TTCATTATAG | AATTCTCCAT | CCAGTCAATG | ATGCATATGG | ATTATGGTTA | 2580 |
| | | | | | | | |

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| | ACGTCAGTTA | TATGCGAGAT | ATGGTTTGCA | GTGTCTTGGA | TTCTTGATCA | ATTCCCCAAA | 2640 |
|----|------------|------------|------------|------------|------------|------------|------|
| | TGGTATCCTA | TAGAACGTGA | AACATACCTC | GATAGACTCT | CTCTCAGGTA | ACATAAACCC | 2700 |
| 5 | TGAAAAGTTC | TTGTCTGCAA | ATATTCATTT | TTTACATTCC | CAAAAATTTT | TGAAACTCTA | 2760 |
| | TTTTTCTTAC | ATAAGGTACG | AGAAGGAAGG | AAAACCGTCA | GGATTAGCAC | CTGTTGATGT | 2820 |
| 10 | TTTTGTTAGT | ACAGTGGATC | CGTTGAAAGA | GCCACCCTTG | ATTACAGCAA | ACACAGTTCT | 2880 |
| 10 | TTCCATTCTA | GCAGTTGATT | ATCCTGTGGA | TAAGGTTGCG | TGTTATGTAT | CAAACAATGG | 2940 |
| | TGCAGCTATG | CTTACATTTG | AAGCTCTCTC | TGATACAGCT | GAGTTTGCTA | GAAAATGGGT | 3000 |
| 15 | TCCTTTTTGT | AAGAAGTTTA | ATATCGAGCC | ACGAGCTCCT | GAGTGGTATT | TTTCTCAGAA | 3060 |
| | GATGGATTAC | CTGAAGAACA | AAGTTCATCC | TGCTTTTGTC | AGGGAACGTC | GTGCTATGAA | 3120 |
| 20 | GGTTTTCTTT | GCTGCTTTTT | CTCTTTCTGA | GTATATCCTA | TCATAAAAGT | GTTGTTTCAA | 3180 |
| 20 | GAATCTGATT | TACGTTTTTT | GCTTGTTTGT | TTGTTGCAGA | GAGATTATGA | GGAGTTTAAA | 3240 |
| | GTGAAGATAA | ATGCACTGGT | TGCTACTGCA | CAGAAAGTGC | CTGAGGAAGG | TTGGACTATG | 3300 |
| 25 | CAAGATGGAA | CTCCTTGGCC | TGGAAACAAC | GTCCGTGACC | ATCCTGGAAT | GATTCAGGTA | 3360 |
| | ATGATGAGTT | TGATTGAATA | GGCAAAAAA | AAGCGGTTTT | TGTCCTCTTC | ACTTTGTTTC | 3420 |
| 30 | CCTGGATCTG | TTAAATTGGA | ATGAGCACTC | TACTTCTCAA | тататсттса | GACCGAAGCC | 3480 |
| | TTTTTAAGAG | ATTTTGTAAA | TGACAGGTGT | TCTTGGGTCA | TAGTGGAGTT | CGTGATACGG | 3540 |
| | ATGGTAATGA | GTTACCACGT | CTAGTGTATG | TTTCTCGTGA | GAAGCGGCCT | GGATTTGATC | 3600 |
| 35 | ACCACAAGAA | AGCTGGAGCT | ATGAATTCCT | TGGTAAGTAT | AATGTGTTTC | TTTATTTATG | 3660 |
| | AATCTCTCTT | TTCGGAGCCC | TGACTTCTCA | ТАЛАСТАЛЛА | CTCATCTTAC | TTCTTCTTGA | 3720 |
| 40 | AGATCCGAGT | CTCTGCTGTT | CTATCAAACG | CTCCTTACCT | TCTTAATGTC | GATTGTGATC | 3780 |
| | | | | | | | |

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| | ACTACATCAA | CAACAGCAAA | GCAATTAGAG | AATCTATGTG | TTTCATGATG | GACCCGCAAT | 3840 |
|----|------------|------------|------------|------------|------------|------------|------|
| | CGGGAAAGAA | AGTTTGTTAT | GTTCAGTTTC | CGCAGAGATT | TGATGGGATT | GATAGACATG | 3900 |
| 5 | ATAGATACTC | AAACCGTAAC | GTTGTGTTCT | TTGATGTATG | TGTCCTTATC | TCTTTTGCTT | 3960 |
| | TGTTTCTGTT | TATGTTTAG | TGCTTTTCCT | CTTTTCTCAT | TTGATATTGT | TTTGGTGTGG | 4020 |
| 10 | AAACAGATTA | ACATGAAAGG | TCTTGATGGG | ATACAAGGAC | CGATATATGT | CGGGACAGGT | 4080 |
| •• | TGTGTGTTTA | GAAAACAGGC | TCTTTATGGT | TTTGATGCAC | CAAAGAAGAA | GAAACCACCA | 4140 |
| | GGCAAAACCT | GTAACTGTTG | GCCTAAATGG | TGTTGTTTGT | GTTGTGGGTT | GAGAAAGAAG | 4200 |
| 15 | AGTAAAACGA | AAGCCAAAGA | TAAGAAAACT | AACACTAAAG | AGACTTCAAA | GCAGATTCAT | 4260 |
| | GCGCTAGAGA | ATGTCGACGA | AGGTGTTATC | GTCCCAGGTA | AAAAAAGAAG | GAAAAAAAA | 4320 |
| 20 | ACATTTCTTA | TTTGGTTTCT | GTCTTGTTGA | AAGTCTAAGT | AGATCCTTTT | GATTGTTAGT | 4380 |
| 20 | GTCAAATGTT | GAGAAGAGAT | CTGAAGCAAC | ACAATTGAAA | TTGGAGAAGA | AGTTTGGACA | 4440 |
| | ATCTCCGGTT | TTCGTTGCCT | CTGCTGTTCT | ACAGAACGGT | GGAGTTCCCC | GTAACGCAAG | 4500 |
| 25 | CCCCGCATGT | TTGTTAAGAG | AAGCCATTCA | AGTTATTAGC | TGCGGGTACG | AAGATAAAAC | 4560 |
| | CGAATGGGGA | AAAGAGGTAG | AAAACATTAC | AAAGTTTTTC | AACTTCTGAA | AACTAGAAAA | 4620 |
| 30 | GTTCTTGTGA | TCTCATTCTT | GCTGATAATC | ACACGCAGAT | CGGGTGGATT | TATGGATCGG | 4680 |
| 50 | TGACTGAAGA | TATCCTGACG | GGTTTCAAGA | TGCATTGCCA | TGGATGGAGA | TCTGTGTACT | 4740 |
| | GTATGCCTAA | GCGTGCAGCT | TTTAAAGGAT | CTGCTCCTAT | TAACTTGTCA | GATCGTCTTC | 4800 |
| 35 | ATCAAGTTCT | ACGTTGGGCT | CTTGGCTCTG | TAGAGATTTT | CTTGAGCAGA | CATTGTCCGA | 4860 |
| | TATGGTATGG | TTATGGTGGT | GGTTTAAAAT | GGTTGGAGAG | ATTCTCTTAC | ATCAACTCTG | 4920 |
| 40 | TCGTCTATCC | TTGGACTTCA | CTTCCATTGA | TCGTCTATTG | TTCTCTCCCC | GCGGTTTGTT | 4980 |
| | | | | | | | |

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5009

| TACTCACAGG | AAAATTCATC | GTCCCTGAG | |
|------------|------------|-----------|--|
|------------|------------|-----------|--|

5 (2) INFORMATION FOR SEQ ID NO:5:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 3603 base pairs

(B) TYPE: nucleic acid

10 (C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

15 (iii) HYPOTHETICAL: NO

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Arabidopsis thaliana

(B) STRAIN: Columbia

20

(vii) IMMEDIATE SOURCE:

(B) CLONE: RSW1 cDNA

(ix) FEATURE:

25 (A) NAME/KEY: CDS

(B) LOCATION: 1..3243

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:

30

ATG GAG GCC AGT GCC GGC TTG GTT GCT GGA TCC TAC CGG AGA AAC GAG 48 Met Glu Ala Ser Ala Gly Leu Val Ala Gly Ser Tyr Arg Arg Asn Glu 1

15

35 CTC GTT CGG ATC CGA CAT GAA TCT GAT GGC GGG ACC AAA CCT TTG AAG Leu Val Arg Ile Arg His Glu Ser Asp Gly Gly Thr Lys Pro Leu Lys

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| | AAT | ATG | TAA | GGC | CAG | ATA | TGT | CAG | ATC | TGT | GGT | GAT | GAT | GTT | GGA | CTC | 144 |
|----|------|-------|------|-----|---------|-------|--------|------------|-----|------|---------|-----|---------|-----|-----|------|-----------|
| | Asn | Met | Asn | Gly | Gln | Ile | Cys | Gln | Ile | Cys | Gly | Asp | Asp | Val | Gly | Leu | |
| | | | 35 | | | | | 40 | | | | | 45 | | | | |
| _ | | | | | | | | | | | | | | | | | |
|) | | | | | | | | GTC | | | | | | | | | 192 |
| | ATA | | Thr | GIY | Asp | Val | | Val | Ala | Cys | Asn | | Cys | Ala | Phe | Pro | |
| | | 50 | | | | | 55 | | | | | 60 | | | | | |
| | GTG | TGT | CGG | ССТ | TGC | TAT | GAG | TAC | GAG | AGG | AAA | GAT | GGA | ACT | CAG | TGT | 240 |
| 10 | | | | | | | | Tyr | | | | | | | | | |
| | 65 | - | _ | | • | 70 | | - | | - | - 75 | - | • | | | 80 | |
| | | | | | | | | | | | | | | | | | |
| | TGC | ССТ | CAA | TGC | AAG | ACT | AGA | TTC | AGA | CGA | CAC | AGG | GGG | AGT | CCT | CGT | 288 |
| | Cys | Pro | Gln | Cys | Lys | Thr | Arg | Phe | Arg | Arg | His | Arg | Gly | Ser | Pro | Arg | |
| 15 | | | | | 85 | | | | | 90 | | | | | 95 | | |
| | | | | | | | | | | | | | | | | | |
| | GTT | GAA | GGA | GAT | GAA | GAT | GAG | GAT | GAT | GTT | GAT | GAT | ATC | GAG | AAT | GAG | 336 |
| | Val | Glu | Gly | - | Glu | Asp | Glu | Asp | - | Val | Asp | Asp | Ile | Glu | Asn | Glu | |
| 20 | | | | 100 | | | | | 105 | | | | | 110 | | | |
| 20 | mmo | * * * | ma c | 000 | | | 000 | | | | | ~~ | | | | | |
| | | | | | | | | AAC Asn | | | | | | | | | 384 |
| | FIIC | ASII | 115 | MIG | 0111 | GIY | ALG | 120 | пув | ATG | ALG | uis | 125 | Arg | nis | GIY | |
| | | | | | | | | 120 | | | | | 123 | | | | |
| 25 | GAA | GAG | TTT | TCT | TCT | TCC | TCT | AGA | CAT | GAA | TCT | CAA | CCA | ATT | CCT | CTT | 432 |
| | | | | | | | | Arg | | | | | | | | | |
| | | 130 | | | | | 135 | | | | | 140 | | | | | |
| | | | | | | | | | | | | | | | | | |
| | CTC | ACC | CAT | GGC | CAT | ACG | GTT | TCT | GGA | GAG | ATT | CGC | ACG | CCT | GAT | ACA | 480 |
| 30 | Leu | Thr | His | Gly | His | Thr | Val | Ser | Gly | Glu | Ile | Arg | Thr | Pro | Asp | Thr | |
| | 145 | | | | | 150 | | | | | 155 | | | | | 160 | |
| | | | | | | | | | | | | | | | | | |
| | | | | | | | | GGT | | | | | | | | | 528 |
| 25 | Gln | Ser | Val | Arg | | Thr | Ser | Gly | Pro | | Gly | Pro | Ser | Asp | Arg | Asn | |
| 35 | | | | | 165 | | | | | 170 | | | | | 175 | | |
| | CCT | יביים | TCA | ጥርጥ | CCA | ጥአጥ | V anax | C N M | CCF | ~~ | C3.2 | | C.T.C | | am. | NCN. | 53 |
| | | | | | | | | GAT Asp | | | | | | | | | 576 |
| | | 210 | 561 | 180 | .10 | - y - | 115 | տոր | 185 | ur A | GIII | 110 | val | 190 | val | wra | |
| | | | | -00 | | | | | 100 | | | | | 130 | | | |

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| | ATC | GTG | GAC | CCG | TCA | AAA | GAC | TTG | AAC | TCT | TAT | GGG | CTT | GGT | AAT | GTT | 624 |
|----|-----|-----|------|-----|----------------|-----|-----|-----|------------|-----|--------------|------|------|-----|-----|-------|------|
| | Ile | Val | Asp | Pro | Ser | Lys | Asp | Leu | Asn | Ser | Tyr | Gly | Leu | Gly | Asn | Val | |
| | | | 195 | | | | | 200 | | | | | 205 | | | | |
| | | | | | | | | | | | | | | | | | |
| 5 | GAC | TGG | AAA | GAA | AGA | GTT | GAA | GGC | TGG | AAG | CTG | AAG | CAG | GAG | AAA | AAT | 672 |
| | Asp | Trp | Lys | Glu | Arg | Val | Glu | Gly | Trp | Lys | Leu | Lys | Gln | Glu | Lys | Asn | |
| | | 210 | | | | | 215 | | | | | 220 | | | | | |
| | | | | | | | | | | | | | | | | | |
| 10 | | | | | ACT | | | | | | | _ | | | | | 720 |
| 10 | | Leu | Gln | Met | Thr | | Lys | Tyr | His | Glu | | Lys | Gly | Gly | Glu | | |
| | 225 | | | | | 230 | | | | | 235 | | | | | 240 | |
| | CAA | ccc | хст | CCT | TCC | እአጥ | ccc | CDD | CAA | ርጥር | ממי | באת | CCT | ርአጥ | ርእጥ | A C A | 768 |
| | | | | | Ser | | | | | | | | | | | | ,00 |
| 15 | GIU | Gly | 1111 | GIY | 245 | Aon | GLY | Giu | 01u | 250 | G1 11 | Mec | ALG | nap | 255 | **** | |
| | | | | | | | | | | | | | | | | | |
| | CGT | CTT | CCT | ATG | AGT | CGT | GTG | GTG | CCT | ATC | CCA | TCT | TCT | CGC | CTA | ACC | 816 |
| | Arg | Leu | Pro | Met | Ser | Arg | Val | Val | Pro | Ile | Pro | Ser | Ser | Arg | Leu | Thr | |
| | _ | | | 260 | | | | | 265 | | | | | 270 | | | |
| 20 | | | | | | | | | | | | | | | | | |
| | CCT | TAT | CGG | GTT | GTG | ATT | ATT | CTC | CGG | CTT | ATC | ATC | TTG | TGT | TTC | TTC | 864 |
| | Pro | Tyr | Arg | Val | Val | Ile | Ile | Leu | Arg | Leu | Ile | Ile | Leu | Cys | Phe | Phe | |
| | | | 275 | | | | | 280 | | | | | 285 | | | | |
| | | | | | | | | | | | | | | | | | |
| 25 | TTG | CAA | TAT | CGT | ACA | ACT | CAC | CCT | GTG | AAA | AAT | GCA | TAT | CCT | TTG | TGG | 912 |
| | Leu | Gln | Tyr | Arg | Thr | Thr | His | Pro | Val | Lys | Aøn | Ala | Tyr | Pro | Leu | Trp | |
| | | 290 | | | | | 295 | | | | | 300 | | | | | |
| | | | | | | | | | | | | | | | | | |
| 30 | | | | | ATC | | | | | | | | | | | | 960 |
| 30 | | inr | ser | vaı | Ile | | GIU | TIE | Trp | Pne | | Pne | ser | Trp | Leu | | |
| | 305 | | | | | 310 | | | | | 315 | | | | | 320 | |
| | TAD | CAG | ידיד | CCC | AAA | TGG | TAC | CCC | ידידע | אמר | AGG | GZG. | ልሮፕ | тат | سس | GAC | 1008 |
| | | _ | | | Lys | | | | _ | | | | | | | | 2000 |
| 35 | | | | | 325 | | -,- | | | 330 | | | •••• | -1- | 335 | | |
| | | | | | - - | | | | | | | | | | | | |
| | CGT | CTC | GCT | ATA | AGA | TAT | GAT | CGA | GAC | GGT | GAA | CCA | TCA | CAG | CTC | GTT | 1056 |
| | Arg | Leu | Ala | Ile | Arg | Tyr | Asp | Arg | Asp | Gly | Glu | Pro | Ser | Gln | Leu | Val | |
| | | | | 340 | | | | | 345 | - | | | | 350 | | | |
| 40 | | | | | | | | | | | | | | | | | |

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| | CCT | GTT | GAT | GTG | TTT | GTT | AGT | ACA | GTG | GAC | CCA | TTG | AAA | GAG | CCT | ccc | 1104 |
|----|------------|------|--------|-----|--------|------------|-----|-----|-----|------|-----|----------|-----|---------|-----|-------|------|
| | Pro | Val | Asp | Val | Phe | Val | Ser | Thr | Val | Asp | Pro | Leu | Lys | Glu | Pro | Pro | |
| | | | 355 | | | | | 360 | | | | | 365 | | | | |
| _ | | | | | | | | | | | | | | | | | |
| 5 | CTT | | | | | | | | | | | | | | | | 1152 |
| | Leu | | Thr | Ala | Asn | Thr | Val | Leu | Ser | Ile | Leu | Ser | Val | Asp | Tyr | Pro | |
| | | 370 | | | | | 375 | | | | | 380 | | | | | |
| | C.T. | ~> m | | | 222 | | | | | | | | | | | | |
| 10 | | | | | | TGT | | | | | | | | | | | 1200 |
| 10 | Val 385 | Asp | Lys | vai | Ala | | туr | vai | ser | Asp | | GIY | Ser | Ala | Met | | |
| | 303 | | | | | 390 | | | | | 395 | | | | | 400 | |
| | ACC | TTT | GAA | TCC | CTT | тст | GAA | ACC | GCT | GAG | ጥጥ | GCA | DAG | 444 | TGG | GTA | 1248 |
| | | | | | | Ser | | | | | | | | | | | 20,0 |
| 15 | | | | | 405 | | | | | 410 | | | -,- | _,, | 415 | 7.4.2 | |
| | | | | | | | | | | | | | | | | | |
| | CCA | TTT | TGC | AAG | AAA | TTC | AAC | ATT | GAA | CCT | AGG | GCC | ССТ | GAA | TTC | TAT | 1296 |
| | Pro | Phe | Сув | Lys | Lys | Phe | Asn | Ile | Glu | Pro | Arg | Ala | Pro | Glu | Phe | Tyr | |
| | | | | 420 | | | | | 425 | | | | | 430 | | | |
| 20 | | | | | | | | | | | | | | | | | |
| | TTT | GCC | CAG | AAG | ATA | GAT | TAC | TTG | AAG | GAC | AAG | ATC | CAA | CCG | TCT | TTT | 1344 |
| | Phe | Ala | Gln | Lys | Ile | Asp | Tyr | Leu | Lys | Asp | Lys | Ile | Gln | Pro | Ser | Phe | |
| | | | 435 | | | | | 440 | | | | | 445 | | | | |
| | | | | | | | | | | | | | | | | | |
| 25 | GTT | | | | | | | | | | | | | | | | 1392 |
| | Val | | Glu | Arg | Arg | Ala | | Lys | Arg | Glu | Tyr | Glu | Glu | Phe | Lys | Val | |
| | | 450 | | | | | 455 | | | | | 460 | | | | | |
| | NCC. | እሞአ | 3 3 TO | | OTT TO | - CORON | 000 | | | ana. | | . | | | | | |
| 30 | Arg | | | | | GTT Val | | | | | | | | | | | 1440 |
| 50 | 465 | 116 | HOII | AIG | Deu | 470 | VIa | Був | Ara | GIII | 475 | 116 | PIO | GIU | GIU | 480 | |
| | | | | | | | | | | | 1/3 | | | | | 460 | |
| | TGG | ACA | ATG | CAG | GAT | GGT | ACT | ccc | TGG | CCT | GGT | AAC | AAC | ACT | AGA | GAT | 1488 |
| | | | | | | Gly | | | | | | | | | | | 2 |
| 35 | • | | | | 485 | - | | | • | 490 | • | | | | 495 | | |
| | | | | | | | | | | | | | | | | | |
| | CAT | CCT | GGA | ATG | ATA | CAG | GTG | TTC | TTA | GGC | CAT | AGT | GGG | GGT | CTG | GAT | 1536 |
| | His | Pro | Gly | Met | Ile | Gln | Val | Phe | Leu | Gly | His | Ser | Gly | Gly | Leu | Asp | |
| | | | | 500 | | | | | 505 | | | | | 510 | | | |
| 40 | | | | | | | | | | | | | | | | | |

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| | ACC | GAT | GGA | AAT | GAG | CTG | CCT | AGA | CTC | ATC | TAT | GTT | TCT | CGT | GAA | AAG | 1584 |
|-----|-----|-------|-------|---------|-------|-----|-----|------|----------|-------|-----|------|------|------|-------------|------|------|
| | Thr | Asp | Gly | Asn | Glu | Leu | Pro | Arg | Leu | Ile | Tyr | Val | Ser | Arg | Glu | Lys | |
| | | | 515 | | | | | 520 | | | | | 525 | | | | |
| | | | | | | | | | | | | | | | | | |
| 5 | CGG | CCT | GGA | TTT | CAA | CAC | CAC | AAA | AAG | GCT | GGA | GCT | ATG | TAA | GCA | TTG | 1632 |
| | Arg | Pro | Gly | Phe | Gln | His | His | Lys | ГЛа | Ala | Gly | Ala | Met | Asn | Ala | Leu | |
| | | 530 | | | | | 535 | | | | | 540 | | | | | |
| | | | | | | | | | | | | | | | | | |
| | | | | | GCT | | | | | | | | _ | _ | | | 1680 |
| 10 | Ile | Arg | Val | Ser | Ala | Val | Leu | Thr | Asn | Gly | Ala | Tyr | Leu | Leu | Asn | Val | |
| | 545 | | | | | 550 | | | | | 555 | | | | | 560 | |
| | | | | | | | | | | | | | | | | | |
| | | | | | TAC | | | | | | | | | | | | 1728 |
| 1.5 | Asp | Cys | Asp | His | Tyr | Phe | Asn | Asn | Ser | • | Ala | Ile | Lys | Glu | | Met | |
| 15 | | | | | 565 | | | | | 570 | | | | | 57 5 | | |
| | mom | mrt C | n mor | N TO CO | C N C | 000 | COM | » mm | CC 3 | B B C | 220 | maa. | maa | m. m | CmC | ara. | 1996 |
| | | | | | GAC | | | | _ | | | | | | | | 1776 |
| | Cys | FIIE | Mec | 580 | Asp | PLO | AId | 116 | 585 | гув | тÅв | cys | Сув | 590 | Val | GIN | |
| 20 | | | | 380 | | | | | 565 | | | | | 390 | | | |
| | TTC | ССТ | CAA | CGT | TTT | GAC | GGT | ΑΤΤ | GAT | TTG | CAC | GAT | A SY | ТАТ | GCC | AAC | 1824 |
| | | | | | Phe | | | | | | | | | | | | 1021 |
| | | | 595 | 3 | | | | 600 | F | | | | 605 | -1- | | | |
| | | | | | | | | | | | | | | | | | |
| 25 | AGG | AAT | ATA | GTC | TTT | TTC | GAT | ATT | AAC | ATG | AAG | GGG | TTG | GAT | GGT | ATC | 1872 |
| | | | | | Phe | | | | | | | | | | | | |
| | | 610 | | | | | 615 | | | | - | 620 | | _ | - | | |
| | | | | | | | | | | | | | | | | | |
| | CAG | GGT | CCA | GTA | TAT | GTG | GGT | ACT | GGT | TGT | TGT | TTT | AAT | AGG | CAG | GCT | 1920 |
| 30 | Gln | Gly | Pro | Val | Tyr | Val | Gly | Thr | Gly | Сув | Cys | Phe | Asn | Arg | Gln | Ala | |
| | 625 | | | | | 630 | | | | | 635 | | | | | 640 | |
| | | | | | | | | | | | | | | | | | |
| | CTA | TAT | GGG | TAT | GAT | CCT | GTT | TTG | ACG | GAA | GAA | GAT | TTA | GAA | CCA | TAA | 1968 |
| | Leu | Tyr | Gly | Tyr | Asp | Pro | Val | Leu | Thr | Glu | Glu | Asp | Leu | Glu | Pro | Asn | |
| 35 | | | | | 645 | | | | | 650 | | | | | 655 | | |
| | | | | | | | | | | | | | | | | | |
| | | | | | AGC | | | | | | | | | | | | 2016 |
| | Ile | Ile | Val | _ | Ser | Сув | Cys | Gly | | Arg | Lys | Lys | Gly | Lys | Ser | Ser | |
| 40 | | | | 660 | | | | | 665 | | | | | 670 | | | |
| 40 | | | | | | | | | | | | | | | | | |

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| | AAG | AAG | TAT | AAC | TAC | GAA | AAG | AGG | AGA | GGC | ATC | AAC | AGA | AGT | GAC | TCC | 2064 |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
| | Lys | Lys | Tyr | Asn | Tyr | Glu | Lys | Arg | Arg | Gly | Ile | Asn | Arg | Ser | Asp | Ser | |
| | | | 675 | | | | | 680 | | | | | 685 | | | | |
| | | | | | | | | | | | | | | | | | |
| 5 | AAT | GCT | CCA | CTT | TTC | AAT | ATG | GAG | GAC | ATC | GAT | GAG | GGT | TTT | GAA | GGT | 2112 |
| | Asn | Ala | Pro | Leu | Phe | Asn | Met | Glu | Asp | Ile | Asp | Glu | Gly | Phe | Glu | Gly | |
| | | 690 | | | | | 695 | | | | | 700 | | | | | |
| | | | | | | | | | | | | | | | | | |
| | TAT | GAT | GAT | GAG | AGG | TCT | ATT | CTA | ATG | TCC | CAG | AGG | AGT | GTA | GAG | AAG | 2160 |
| 10 | Tyr | Asp | Asp | Glu | Arg | Ser | Ile | Leu | Met | Ser | Gln | Arg | Ser | Val | Glu | Lys | |
| | 705 | | | | | 710 | | | | | 715 | | | | | 720 | |
| | | | | | | | | | | | | | | | | | |
| | CGT | TTT | GGT | CAG | TCG | CCG | GTA | TTT | ATT | GCG | GCA | ACC | TTC | ATG | GAA | CAA | 2208 |
| | Arg | Phe | Gly | Gln | Ser | Pro | Val | Phe | Ile | Ala | Ala | Thr | Phe | Met | Glu | Gln | |
| 15 | | | | | 725 | | | | | 730 | | | | | 735 | | |
| | | | | | | | | | | | | | | | | | |
| | GGÇ | GGC | ATT | CCA | CCA | ACA | ACC | AAT | CCC | GCT | ACT | CTT | CTG | AAG | GAG | GCT | 2256 |
| | Gly | Gly | Ile | Pro | Pro | Thr | Thr | Asn | Pro | Ala | Thr | Leu | Leu | Lys | Glu | Ala | |
| | | | | 740 | | | | | 745 | | | | | 750 | | | |
| 20 | | | | | | | | | | | | | | | | | |
| | ATT | CAT | GTT | ATA | AGC | TGT | GGT | TAC | GAA | GAC | AAG | ACT | GAA | TGG | GGC | AAA | 2304 |
| | Ile | His | Val | Ile | Ser | Cys | Gly | Tyr | Glu | Asp | Lys | Thr | Glu | Trp | Gly | Lys | |
| | | | 755 | | | | | 760 | | | | | 765 | | | | |
| | | | | | | | | | | | | | | | | | |
| 25 | GAG | ATT | GGT | TGG | ATC | TAT | GGT | TCC | GTG | ACG | GAA | GAT | ATT | CTT | ACT | GGG | 2352 |
| | Glu | Ile | Gly | Trp | Ile | Tyr | Gly | Ser | Val | Thr | Glu | Asp | Ile | Leu | Thr | Gly | |
| | | 770 | | | | | 775 | | | | | 780 | | | | | |
| | | | | | | | | | | | | | | | | | |
| | TTC | AAG | ATG | CAT | GCC | CGG | GGT | TGG | ATA | TCG | ATC | TAC | TGC | AAT | CCT | CCA | 2400 |
| 30 | Phe | Lys | Met | His | Ala | Arg | Gly | Trp | Ile | Ser | Ile | Tyr | Сув | Asn | Pro | Pro | |
| | 785 | | | | | 790 | | | | | 795 | | | | | 800 | |
| | | | | | | | | | | | | | | | | | |
| | CGC | CCT | GCG | TTC | AAG | GGA | TCT | GCA | CCA | ATC | AAT | CTT | TCT | GAT | CGT | TTG | 2448 |
| | Arg | Pro | Ala | Phe | Lys | Gly | Ser | Ala | Pro | Ile | Asn | Leu | Ser | Asp | Arg | Leu | |
| 35 | | | | | 805 | | | | | 810 | | | | | 815 | | |
| | | | | | | | | | | | | | | | | | |
| | AAC | CAA | GTT | CTT | CGA | TGG | GCT | TTG | GGA | TCT | ATC | GAG | ATT | CTT | CTT | AGC | 2496 |
| | Asn | Gln | Val | Leu | Arg | Trp | Ala | Leu | Gly | Ser | Ile | Glu | Ile | Leu | Leu | Ser | |
| | | | | 820 | | | | | 825 | | | | | 830 | | | |
| | | | | | | | | | | | | | | | | | |

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| | AGA | CAT | TGT | CCT | ATC | TGG | TAT | GGT | TAC | CAT | GGA | AGG | TTG | AGA | CTT | TTG | 2544 |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
| | Arg | His | Cys | Pro | Ile | Trp | Tyr | Gly | Tyr | His | Gly | Arg | Leu | Arg | Leu | Leu | |
| | | | 835 | | | | | 840 | | | | | 845 | | | | |
| | | | | | | | | | | | | | | | | | |
| 5 | GAG | AGG | ATC | GCT | TAT | ATC | AAC | ACC | ATC | GTC | TAT | CCT | ATT | ACA | TCC | ATC | 2592 |
| | Glu | Arg | Ile | Ala | Tyr | Ile | Asn | Thr | Ile | Val | Tyr | Pro | Ile | Thr | Ser | Ile | |
| | | 850 | | | | | 855 | | | | | 860 | | | | | |
| | | | | | | | | | | | | | | | | | |
| | CCT | CTT | ATT | GCG | TAT | TGT | ATT | CTT | CCC | GCT | TTT | TGT | CTC | ATC | ACC | GAC | 2640 |
| 10 | Pro | Leu | Ile | Ala | Tyr | Cys | Ile | Leu | Pro | Ala | Phe | Сув | Leu | Ile | Thr | Asp | |
| | 865 | | | | | 870 | | | | | B75 | | | | | 880 | |
| | | | | | | | | | | | | | | | | | |
| | AGA | TTC | ATC | ATA | CCC | GAG | ATA | AGC | AAC | TAC | GCG | AGT | ATT | TGG | TTC | ATT | 2688 |
| | Arg | Phe | lle | Ile | Pro | Glu | Ile | Ser | naA | Tyr | Ala | Ser | Ile | Trp | Phe | Ile | |
| 15 | | | | | 885 | | | | | 890 | | | | | 895 | | |
| | | | | | | | | | | | | | | | | | |
| | CTA | CTC | TTC | ATC | TCA | ATT | GCT | GTG | ACT | GGA | ATC | CTG | GAG | CTG | AGA | TGG | 2736 |
| | Leu | Leu | Phe | Ile | Ser | Ile | Ala | Val | Thr | Gly | Ile | Leu | Glu | Leu | Arg | Trp | |
| | | | | 900 | | | | | 905 | | | | | 910 | | | |
| 20 | | | | | | | | | | | | | | | | | |
| | AGC | GGT | GTG | AGC | ATT | GAG | GAT | TGG | TGG | AGG | AAC | GAG | CAG | TTC | TGG | GTC | 2784 |
| | Ser | Gly | Val | Ser | Ile | Glu | Asp | Trp | Trp | Arg | Asn | Glu | Gln | Phe | Trp | Val | |
| | | | 915 | | | | | 920 | | | | | 925 | | | | |
| | | | | | | | | | | | | | | | | | |
| 25 | ATT | GGT | GGC | ACA | TCC | GCC | CAT | CTT | TTT | GCT | GTC | TTC | CAA | GGT | CTA | CTT | 2832 |
| | Ile | Gly | Gly | Thr | Ser | Ala | His | Leu | Phe | Ala | Val | Phe | Gln | Gly | Leu | Leu | |
| | | 930 | | | | | 935 | | | | | 940 | | | | | |
| | | | | | | | | | | | | | | | | | |
| | AAG | GTT | CTT | GCT | GGT | ATC | GAC | ACC | AAC | TTC | ACC | GTT | ACA | TCT | AAA | GCC | 2880 |
| 30 | Lys | Val | Leu | Ala | Gly | Ile | Asp | Thr | Asn | Phe | Thr | Val | Thr | Ser | rys | Ala | |
| | 945 | | | | | 950 | | | | | 955 | | | | | 960 | |
| | | | | | | | | | | | | | | | | | |
| | ACA | GAC | GAA | GAT | GGG | GAT | TTT | GCA | GAA | CTC | TAC | ATC | TTC | AAA | TGG | ACA | 2928 |
| | Thr | Asp | Glu | Asp | Gly | Asp | Phe | Ala | Glu | Leu | Tyr | Ile | Phe | Lys | Trp | Thr | |
| 35 | | | | | 965 | | | | | 970 | | | | | 975 | | |
| | | | | | | | | | | | | | | | | | |
| | GCT | CTT | CTC | ATT | CCA | CCA | ACC | ACC | GTC | CTA | CTT | GTG | AAC | CTC | ATA | GGC | 2976 |
| | Ala | Leu | Leu | Ile | Pro | Pro | Thr | Thr | Val | Leu | Leu | Val | Asn | Leu | Ile | Gly | |
| | | | | 980 | | | | | 985 | | | | | 990 | | | |

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| | ATT | GTG | GCT | GGT | GTC | TCT | TAT | GCT | GTA | AAC | AGT | GGC | TAC | CAG | TCG | TGG | 3024 |
|-----|---------|-------------|--------|------------|-------|---------|-------|--------------|------------|----------|---------|--------|----------|---------|-------|--------|------|
| | Ile | Val | Ala | Gly | Val | Ser | Tyr | Ala | Val | Asn | Ser | Gly | Tyr | Gln | Ser | Trp | |
| | | | 995 | | | | | 1000 |) | | | | 1009 | 5 | | | |
| _ | | | | | | | | | | | | | | | | | |
| 5 | GGT | CCG | CTT | TTC | GGG | AAG | CTC | TTC | TTC | GCC | ATT | TGG | GTT | ATT | GCC | CAT | 3072 |
| | Gly | Pro | Leu | Phe | Gly | Lys | Leu | Phe | Phe | Ala | Leu | Trp | Val | Ile | Ala | His | |
| | | 1010 | 0 | | | | 1019 | 5 | | | | 1020 | 0 | | | | |
| | | | | | | | | | | | | | | | | | |
| •• | | | | TTC | | | | | | | | | | | | | 3120 |
| 10 | | | Pro | Phe | Leu | | | Leu | Leu | Gly | Arg | Gln | Asn | Arg | Thr | Pro | |
| | 1029 | 5 | | | | 103 |) | | | | 103 | 5 | | | | 1040 | |
| | | | | | | | | | | | | | | | | | |
| | | | | TTA | | | | | | | | | | | | | 3168 |
| 1.5 | Thr | Ile | Val | Ile | | - | Ser | Val | Leu | | | Ser | Ile | Phe | | | |
| 15 | | | | | 1049 | 5 | | | | 1050 |) | | | | 105 | 5 | |
| | C th th | mac. | C.D.C. | 200 | 2 mc | * * * * | 200 | | ama | ~ | | | 222 | | | | 2016 |
| | | | | AGG | | | | | | | | | | | | | 3216 |
| | Leu | irp | vaı | Arg 106 | | Asn | PIO | Pne | 106 | • | Ala | Asn | Pro | 107 | | Asn | |
| 20 | | | | 1000 | J | | | | 106 | • | | | | 107 | U | | |
| -0 | חממ | ተተ ር | דממ | GGC | מממ | GCA | CCT | GTC | July Trans | ጥልር፡ | מ ריריי | י ידמי | ייי אייי | ስ ሞ አ 🦳 | TVT | | 3263 |
| | | | | Gly | | | | | | IAGI | 1000 | ını | 11711 | AIAC | | | 3203 |
| | AGII | **** | 107 | • | Dy 5 | O.y | GLY | 108 | | | | | | | | | |
| | | | 107 | _ | | | | 100 | | | | | | | | | |
| 25 | GTG' | rgrg | CAT | ATAT | CAAA | AA C | GCGC | AATG | G GA | ATTC | AAA | TCA' | тста | אאר ו | CCAT | CAAACC | 3323 |
| | | | | | | | | | | | | | | | | | - |
| | CCA | GTGA | ACC (| GGGC | AGTT | AA G | GTGA: | TTCC | A TG | rcca: | AGAT | TAG | CTTT | CTC | CGAG' | PAGCCA | 3383 |
| | | | | | | | | | | | | | | | | | |
| | GAG | AAGG' | TGA . | AATT | GTTC | GT A | ACAC | TATT | G TA | ATGA' | TTTT | CCA | GTGG | GGA . | AGAA | GATGTG | 3443 |
| 30 | | | | | | | | | | | | | | | | | |
| | GAC | CCAA | ATG . | ATAC | ATAG' | TC T | ACAA | AA AG | A AT | TTGT | TATT | CTT | TCTT | ATA | TTTA' | TATTT | 3503 |
| | | | | | | | | | | | | | | | | | |
| | TTA | AAGC | TTG | TTAG | ACTC | AC A | CTTA' | TGTA | A TG | rtgg. | AACT | TGT | TGTC | CTA. | AAAA | GGATT | 3563 |
| | | | | | | | | | | | | | | | | | |
| 35 | GGA | GTTT | TCT | TTTT. | ATCT | AA G | AATC | TGAA | G TT | TATA' | TGCT | | | | | | 3603 |
| | | | | | | | | | | | | | | | | | |

(2) INFORMATION FOR SEQ ID NO:6:

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| | | | | (A) | LE | NGTH | : 10 | 81 at | nino | aci | ds | | | | | |
|----|------------|------------|------------|-----------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|-----------|
| | | | | (B | TY! | PE: a | amino | ac | id | | | | | | | |
| | | | | (D | TO | POLO | GY: : | line | ar | | | | | | | |
| 5 | | (. | ii) t | MOLE | CULE | TYP | E: p | rote: | in | | | | | | | |
| | | (: | xi} s | SEQUI | ENCE | DES | CRIP: | rion | : SE(| Q ID | NO: | 5 : | | | | |
| 10 | Met 1 | Glu | Ala | Ser | Ala 5 | Gly | Leu | Val | Ala | Gly 10 | Ser | Tyr | Arg | Arg | Asn 15 | Glu |
| | Leu | Val | Arg | Ile 20 | Arg | Н13 | Glu | Ser | Asp 25 | Gly | Gly | Thr | Lys | Pro 30 | Leu | Lys |
| 15 | Asn | Met | Asn 35 | Gly | Gln | Ile | Суз | Gln 40 | Ile | Сув | Gly | Asp | Asp 45 | Val | Gly | Leu |
| | Ala | Glu 50 | Thr | Gly | Asp | Val | Phe 55 | Val | Ala | Сув | Asn | Glu 60 | Сув | Ala | Phe | Pro |
| 20 | Val 65 | Cys | Arg | Pro | Cys | Tyr 70 | Glu | Tyr | Glu | Arg | Lys 75 | Asp | Gly | Thr | Gln | Су: 80 |
| 25 | Cys | Pro | Gln | Cys | Lys 85 | Thr | Arg | Phe | Arg | Arg 90 | His | Arg | Gly | Ser | Pro 95 | Arg |
| | Val | Glu | Gly | Asp | Glu | Asp | Glu | Asp | Asp 105 | Val | Asp | Asp | Ile | Glu 110 | Asn | Glu |
| 30 | Phe | Asn | Tyr 115 | Ala | Gln | Gly | Ala | Asn 120 | Lys | Ala | Arg | His | Gln 125 | Arg | His | Gly |
| 35 | Glu | Glu 130 | Phe | Ser | Ser | Ser | Ser 135 | Arg | His | Glu | Ser | Gln 140 | Pro | Ile | Pro | Leu |
| 3 | Leu 145 | Thr | His | Gly | His | Thr 150 | Val | Ser | Gly | Glu | Ile 155 | Arg | Thr | Pro | Asp | Th: |
| 40 | Gln | Ser | Val | Arg | Thr 165 | Thr | Ser | Gly | Pro | Leu 170 | Gly | Pro | Ser | Asp | Arg 175 | Ası |

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| Ala | Ile | Ser | Ser | Pro | Tyr | Ile | Asp | Pro | Arg | Gln | Pro | Val | Pro | Val | Arg |
|-----|-------------------------------------|---|--|---|---|--|--|---|--|--|---|---|---|---|---|
| | | | 180 | | | | | 185 | | | | | 190 | | |
| | | | | | | | | | | | | | | | |
| Ile | Val | Asp | Pro | Ser | Lys | Asp | Leu | Asn | Ser | Tyr | Gly | Leu | Gly | Asn | Val |
| | | 195 | | | | | 200 | | | | | 205 | | | |
| | | | | | | | | | | | | | | | |
| Asp | Trp | Lys | Glu | Arg | Val | Glu | Gly | Trp | Lys | Leu | Lys | Gln | Glu | Lys | Asn |
| | 210 | | | | | 215 | | | | | 220 | | | | |
| | | | | | | | | | | | | | | | |
| Met | Leu | Gln | Met | Thr | Gly | Lys | Tyr | His | Glu | Gly | Lys | Gly | Gly | Glu | Ile |
| 225 | | | | | 230 | | | | | 235 | | | | | 240 |
| | | | | | | | | | | | | | | | |
| Glu | Gly | Thr | Gly | Ser | Asn | Gly | Glu | Glu | Leu | Gln | Met | Ala | Asp | Asp | Thr |
| | | | | 245 | | | | | 250 | | | | | 255 | |
| | | | | | | | | | | | | | | | |
| Arg | Leu | Pro | Met | Ser | Arg | Val | Val | Pro | Ile | Pro | Ser | Ser | Arg | Leu | Thr |
| | | | 260 | | | | | 265 | | | | | 270 | | |
| | | | | | | | | | | | | | | | |
| Pro | Tyr | Arg | Val | Val | Ile | Ile | Leu | Arg | Leu | Ile | Ile | Leu | Cys | Phe | Phe |
| | | 275 | | | | | 280 | | | | | 285 | | | |
| | | | | | | | | | | | | | | | |
| Leu | Gln | Tyr | Arg | Thr | Thr | His | Pro | Val | Lys | Asn | Ala | Tyr | Pro | Leu | Trp |
| | 290 | | | | | 295 | | | | | 300 | | | | |
| | | | | | | | | | | | | | | | |
| Leu | Thr | Ser | Val | Ile | Сув | Glu | Ile | Trp | Phe | Ala | Phe | Ser | Trp | Leu | Leu |
| 305 | | | | | 310 | | | | | 315 | | | | | 320 |
| | | | | | | | | | | | | | | | |
| Asp | Gln | Phe | Pro | Lys | Trp | Tyr | Pro | Ile | Asn | Arg | Glu | Thr | Tyr | Leu | qaA |
| | | | | 325 | | | | | 330 | | | | | 335 | |
| | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | |
| Arg | Leu | Ala | Ile | Arg | Tyr | Asp | Arg | Asp | Gly | Glu | Pro | Ser | Gln | Leu | Val |
| Arg | Leu | Ala | Ile 340 | Arg | Tyr | Asp | Arg | Asp 345 | Gly | Glu | Pro | Ser | Gln 350 | Leu | Val |
| Arg | Leu | Ala | | Arg | Tyr | Asp | Arg | | Gly | Glu | Pro | Ser | | Leu | Val |
| | | | 340 | Arg | | | | 345 | | | | | 350 | | |
| | | | 340 | | | | | 345 | | | | | 350 | | |
| | | Asp | 340 | | | | Thr | 345 | | | | Lys | 350 | | |
| Pro | Val | Asp 355 | 340 Val | | Val | Ser | Thr 360 | 345 Val | Авр | Pro | Leu | Lys 365 | 350 Glu | Pro | Pro |
| | Ile Asp Met 225 Glu Arg Pro Leu Jo5 | Ile Val Asp Trp 210 Met Leu 225 Glu Gly Arg Leu Pro Tyr Leu Gln 290 Leu Thr 305 | Ile Val Asp 195 Asp Trp Lys 210 Met Leu Gln 225 Glu Gly Thr Arg Leu Pro Pro Tyr Arg 275 Leu Gln Tyr 290 Leu Thr Ser 305 | 11e Val Asp Pro 195 Lys Glu Asp Trp Lys Glu Met Leu Gln Met 225 Thr Gly Glu Gly Thr Gly Arg Leu Pro Met 260 Pro Tyr Arg Val 275 Leu Gln Tyr Arg Arg Leu Thr Ser Val 305 Thr Ser Val | 11e Val Asp Pro Ser 195 Pro Ser Asp Trp Lys Glu Arg Met Leu Gln Met Thr Glu Gly Thr Gly Ser Arg Leu Pro Met Ser 260 Pro Met Pro Leu Gln Tyr Arg Val Val Leu Thr Ser Val Ile Jos Gln Phe Pro Lys | 180 Tite Asp 195 Pro Ser Lys Asp 210 Lys Glu Arg Val Met Leu Gln Met Thr Gly 230 Glu Gly Thr Gly Ser Asn 245 Arg Leu Pro Met Ser Arg 260 Pro Tyr Arg Val Val Ile 275 Leu Gln Tyr Arg Thr Thr 290 Leu Thr Ser Val Ile Cys 305 Asp Gln Phe Pro Lys Trp | 180 11e Val Asp 195 Pro Ser Lys Asp 215 Asp 210 Lys Glu Arg Val Glu 215 Met 220 Leu Gln Met Thr Gly 230 Lys Glu Gly Thr Gly 245 Asp 230 Gly 245 Arg 230 Fr Arg Leu Pro Met 260 Ser 245 Arg 241 Fr Fr Val Ile < | 180 11e Val Asp Pro Ser Lys Asp Leu Asp Trp Lys Glu Arg Val Glu Gly Met Leu Gln Met Thr Gly Lys Tyr 225 Thr Gly Ser Asn Gly Glu Glu Gly Thr Gly Ser Asn Gly Glu Arg Leu Pro Met Ser Arg Val Val Pro Tyr Arg Val Val Ile Ile Leu Leu Gln Tyr Arg Thr Thr His Pro Leu Thr Ser Val Ile Cys Glu Ile Asp Gln Phe Pro Lys Trp Tyr Pro | 11e Val Asp 195 Pro 295 Lys 200 Asp 200 Arp 200 Arp 2015 Arp 2015 Arp 2015 Arp 2015 Arp 2015 Arp 2015 Arp 2010 Ar | 180 185 185 11e Val Asp Pro Ser Lys Asp Leu Asn Ser Asp Trp Lys Glu Arg Val Glu Gly Trp Lys Amet Leu Gln Met Thr Gly Lys Tyr His Glu Glu Gly Thr Gly Ser Asn Gly Glu His Glu Leu Arg Leu Pro Met Ser Arg Val Val Pro Pro Leu Arg Tyr Arg Val Val Ile Leu Arg Leu Leu Gln Tyr Arg Thr Thr His Pro Val Lys Leu Thr Ser Val Ile Cys Glu Ile Trp Phe 305 Tyr Pro Ile Asn Tyr Pro Ile Asn | 180 185 TIR Val Asp pro 195 Ser Lys Asp pro 200 Asp pro 200 Ser Tyr pro 200 Asp Trp Lys Lys Pro 210 Pro 210 Pro 215 Pro 215 <td> 180 185 185 187 187 187 187 187 188 189</td> <td> 180 185 185 186 185 185 197 198 195</td> <td> 180 180 190</td> <td> The Val Asp Pro Ser Lys Asp Leu Asn Ser Tyr Gly Leu Gly Asn 200</td> | 180 185 185 187 187 187 187 187 188 189 | 180 185 185 186 185 185 197 198 195 | 180 180 190 | The Val Asp Pro Ser Lys Asp Leu Asn Ser Tyr Gly Leu Gly Asn 200 |

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| | | 385 | Asp | Lys | Val | AIA | 390 | Tyr | Val | ser | Asp | 395 | GIĀ | ser | Ala | Met | 400 |
|---|----|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|--------------------|------------|------------|------------|------------|------------|
| | 5 | Thr | Phe | Glu | Ser | Leu 405 | Ser | Glu | Thr | Ala | Glu 410 | Phe | Ala | Lys | Lys | Trp 415 | Val |
| | | Pro | Phe | Cys | Lys 420 | Lys | Phe | Asn | Ile | Glu 425 | Pro | Arg | Ala | Pro | Glu 430 | Phe | Туг |
| | 10 | Phe | Ala | Gln 435 | Lys | Ile | Asp | Tyr | Leu 440 | Lys | Asp | Lys | Ile | Gln 445 | Pro | Ser | Phe |
| | 15 | Val | Lys 450 | Glu | Arg | Arg | Ala | Met 455 | Lys | Arg | Glu | Tyr | Glu 460 | Glu | Phe | Lys | Val |
| | | Arg 465 | Ile | Asn | Ala | Leu | Val 470 | Ala | Lys | Ala | Gln | L ув 475 | Ile | Pro | Glu | Glu | Gly 480 |
| ; | 20 | Trp | Thr | Met | Gln | Asp 485 | Gly | Thr | Pro | Trp | Pro 490 | Gly | Asn | Asn | Thr | Arg 495 | Asp |
| | | His | Pro | Gly | Met 500 | Ile | Gln | Val | Phe | Leu 505 | Gly | His | Ser | Gly | Gly 510 | Leu | Asp |
| ; | 25 | Thr | Asp | Gly 515 | Asn | Glu | Leu | Pro | Arg 520 | Leu | Ile | Tyr | Val | Ser 525 | Arg | Glu | Lys |
| : | 30 | Arg | Pro 530 | Gly | Phe | Gln | His | His 535 | Lys | Lys | Ala | Gly | Ala 540 | Met | Asn | Ala | Leu |
| | | Ile 545 | Arg | Val | Ser | Ala | Val 550 | Leu | Thr | Asn | Gly | Ala 555 | Tyr | Leu | Leu | Asn | Val |
| | 35 | Asp | Cys | Asp | His | Tyr 565 | Phe | Asn | Asn | Ser | Lys 570 | Ala | Ile | Lys | Glu | Ala 575 | Met |
| | | Сув | Phe | Met | Met 580 | Авр | Pro | Ala | Ile | Gly 585 | Lys | Lys | Сув | Сув | Tyr 590 | Val | Gln |

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| | Phe | Pro | Gln | Arg | Phe | Asp | Gly | Ile | Asp | Leu | His | Asp | Arg | Tyr | Ala | Asn |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| | | | 595 | | | | | 600 | | | | | 605 | | | |
| | | | | | | | | | | | | | | | | |
| | Arg | Asn | Ile | Val | Phe | Phe | Asp | Ile | Asn | Met | Lys | Gly | Leu | Asp | Gly | Ile |
| 5 | | 610 | | | | | 615 | | | | | 620 | | | | |
| | | | | | | | | | | | | | | | | |
| | Gln | Gly | Pro | Val | Tyr | Val | Gly | Thr | Gly | Cys | Cys | Phe | Asn | Arg | Gln | Ala |
| | 625 | | | | | 630 | | | | | 635 | | | | | 640 |
| | | | | | | | | | | | | | | | | |
| 10 | Leu | Tyr | Gly | Tyr | Asp | Pro | Val | Leu | Thr | Glu | Glu | Asp | Leu | Glu | Pro | Asn |
| | | | | | 645 | | | | | 650 | | | | | 655 | |
| | | | | | | | | | | | | | | | | |
| | Ile | Ile | Val | Lys | Ser | Cys | Сув | Gly | Ser | Arg | Lys | Lys | Gly | Lys | Ser | Ser |
| | | | | 660 | | | | | 665 | | | | | 670 | | |
| 15 | | | | | | | | | | | | | | | | |
| | Lys | Lys | Tyr | Asn | Tyr | Glu | Lys | Arg | Arg | Gly | Ile | Asn | Arg | Ser | Авр | Ser |
| | | | 675 | | | | | 680 | | | | | 685 | | | |
| | | | | | | | | | | | | | | | | |
| | Asn | Ala | Pro | Leu | Phe | Asn | Met | Glu | Asp | Ile | Asp | Glu | Gly | Phe | Glu | Gly |
| 20 | | 690 | | | | | 695 | | | | | 700 | | | | |
| | | | | | | | | | | | | | | | | |
| | Tyr | Asp | Asp | Glu | Arg | Ser | Ile | Leu | Met | Ser | Gln | Arg | Ser | Val | Glu | Lys |
| | 705 | | | | | 710 | | | | | 715 | | | | | 720 |
| | | | | | | | | | | | | | | | | |
| 25 | Arg | Phe | Gly | Gln | Ser | Pro | Val | Phe | Ile | Ala | Ala | Thr | Phe | Met | Glu | Gln |
| | | | | | 725 | | | | | 730 | | | | | 735 | |
| | | | | | | | | | | | | | | | | |
| | Gly | Gly | Ile | Pro | Pro | Thr | Thr | Asn | Pro | Ala | Thr | Leu | Leu | Lys | Glu | Ala |
| | | | | 740 | | | | | 745 | | | | | 750 | | |
| 30 | | | | | | | | | | | | | | | | |
| | Ile | His | Val | Ile | Ser | Сув | Gly | Tyr | Glu | Asp | Lys | Thr | Glu | Trp | Gly | Lys |
| | | | 755 | | | | | 760 | | | | | 765 | | | |
| | | | | | | | | | | | | | | | | |
| | Glu | Ile | Gly | Trp | Ile | Tyr | Gly | Ser | Val | Thr | Glu | Asp | Ile | Leu | Thr | Gly |
| 35 | | 770 | | | | | 775 | | | | | 780 | | | | |
| | | | | | | | | | | | | | | | | |
| | Phe | Lys | Met | His | Ala | Arg | Gly | Trp | Ile | Ser | Ile | Tyr | Сув | Asn | Pro | Pro |
| | 785 | | | | | 790 | | | | | 795 | | | | | 800 |

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| | Arg | Pro | Ala | Phe | Lys 805 | Gly | Ser | Ala | Pro | Ile 810 | Asn | Leu | Ser | Asp | Arg 815 | Leu |
|----|------------|------------|------------|------------|--------------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| 5 | Asn | Gln | Val | Leu 820 | Arg | Trp | Ala | Leu | Gly 825 | Ser | Ile | Glu | Ile | Leu 830 | Leu | Ser |
| | Arg | His | Cys 835 | Pro | Ile | Trp | Tyr | Gly 840 | Tyr | His | Gly | Arg | Leu 845 | Arg | Leu | Leu |
| 10 | Glu | Arg 850 | Ile | Ala | Tyr | Ile | Asn 855 | Thr | Ile | Val | Tyr | Pro 860 | Ile | Thr | Ser | Ile |
| 15 | Pro 865 | Leu | Ile | Ala | туг | Cys 870 | Ile | Leu | Pro | Ala | Phe 875 | Cys | Leu | Ile | Thr | Asp |
| | Arg | Phe | Ile | Ile | Pro 885 | Glu | Ile | Ser | Asn | Tyr 890 | Ala | Ser | Ile | Trp | Phe 895 | Ile |
| 20 | Leu | Leu | Phe | 11e 900 | Ser | Ile | Ala | Val | Thr 905 | Gly | Ile | Leu | Glu | Leu 910 | Arg | Trp |
| | Ser | Gly | Val 915 | Ser | Ile | G1u | Asp | Trp 920 | Trp | Arg | Asn | Glu | Gln 925 | Phe | Trp | Val |
| 25 | Ile | Gly 930 | Gly | Thr | Ser | Ala | His 935 | Leu | Phe | Ala | Val | Phe 940 | Gln | Gly | Leu | Leu |
| 30 | Lys 945 | Val | Leu | Ala | Gly | Ile 950 | Asp | Thr | Asn | Phe | Thr 955 | Val | Thr | Ser | Lys | Ala 960 |
| | Thr | Asp | Glu | Asp | Gl <i>y</i> 965 | Asp | Phe | Ala | Glu | Leu 970 | туг | Ile | Phe | Lys | Trp 975 | Thr |
| 35 | Ala | Leu | Leu | Ile 980 | Pro | Pro | Thr | Thr | Val 985 | Leu | Leu | Val | Asn | Leu 990 | Ile | Gly |
| | Ile | Val | Ala | Gly | Val | Ser | Tyr | Ala | | Asn | Ser | Gly | Tyr | | Ser | Trp |

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Gly Pro Leu Phe Gly Lys Leu Phe Phe Ala Leu Trp Val Ile Ala His 1015 Leu Tyr Pro Phe Leu Lys Gly Leu Leu Gly Arg Gln Asn Arg Thr Pro 5 1025 1030 1035 Thr Ile Val Ile Val Trp Ser Val Leu Leu Ala Ser Ile Phe Ser Leu 1045 1050 10 Leu Trp Val Arg Ile Asn Pro Phe Val Asp Ala Asn Pro Asn Ala Asn 1060 1065 1070 Asn Phe Asn Gly Lys Gly Gly Val Phe 1075 1080 15 (2) INFORMATION FOR SEQ ID NO:7: 20 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 3828 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear 25 (ii) MOLECULE TYPE: cDNA (iii) HYPOTHETICAL: NO 30 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (A) ORGANISM: Arabidopsis thaliana (B) STRAIN: Columbia 35 (vii) IMMEDIATE SOURCE: (B) CLONE: Ath-A (ix) FEATURE:

40

(A) NAME/KEY: CDS

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(B) LOCATION: 239..3490

| 5 | | (xi) |) SE(| QUENC | CE DI | ESCR | IPTI(| ON: S | SEQ : | ID NO | 0:7: | | | | | | | |
|----|----------|---------------|-------|-------|----------|-------|-------|---------------|-------|-----------|------|-----|-------|-------|-----------|--------|---|-----|
| J | GTC | GACA | CTA A | AGTG | GATC | CA AJ | AGAA | TCG | C GG | cccc | STCG | ATA | CGC. | rgc (| GAGAJ | AGACGA | 4 | 60 |
| | CAG | \A GG(| GGA ' | rtgto | CGAT' | rc Go | GTTT | \TT T(| C GT | CTCC | rtcg | TCT | rcca | CTC ' | l'Tac' | ragtg(| 2 | 120 |
| 10 | ATG | CTCT | GAA 1 | rctg: | ratg: | ra at | rgggi | AGTT(| C AA | CAGT | CTGG | ATC | CATT | ATC (| CTAG | ccggg1 | r | 180 |
| | CGGC | STCA | AGG 1 | rctt: | rgaa' | ra ac | GAGA(| GACA | A TT | CGTT | rtga | TTC | GGTG: | rag i | AAGA(| CATC | | 238 |
| | | | | GGT | | | | | | | | | | | | | | 286 |
| 15 | Met 1 | Asn | Thr | Gly | Gly 5 | Arg | Leu | Ile | Ala | Gly 10 | Ser | His | Asn | Arg | Asn 15 | Glu | | |
| | _ | | | | | | | | | | | | | | | | | |
| | TTC | GTT | CTC | ATT | AAC | GCC | GAT | GAG | AGT | GCC | AGA | ATA | CGA | TCA | GTA | CAA | | 334 |
| | Phe | Val | Leu | Ile | Asn | Ala | Asp | Glu | Ser | Ala | Arg | Ile | Arg | Ser | Val | Gln | | |
| 20 | | | | 20 | | | | | 25 | | | | | 30 | | | | |
| | GAA | CTG | AGT | GGG | CAA | ACA | TGT | CAA | ATC | TGT | GGA | GAT | GAA | ATC | GAA | TTA | | 382 |
| | Glu | Leu | Ser | Gly | Gln | Thr | Cys | Gln | Ile | Сув | Gly | Asp | Glu | Ile | Glu | Leu | | |
| 25 | | | 35 | | | | | 40 | | | | | 45 | | | | | |
| 23 | ACG | GTT | AGC | AGT | DAD | CTC | ጥጥ | GTT | GCT | TGC | DAC | GAA | TGC | GCA | ттс | CCG | | 430 |
| | | | | Ser | | | | | | | | | | | | | | |
| | | 50 | | | | | 55 | | | | | 60 | | | | | | |
| | | | | | | | | | | | | | | | | | | |
| 30 | _ | | | CCA | | | _ | | _ | | | | | | | | | 478 |
| | | Сув | Arg | Pro | Cys | _ | Glu | Tyr | Glu | Arg | _ | Glu | Gly | Asn | Gln | | | |
| | 65 | | | | | 70 | | | | | 75 | | | | | 80 | | |
| | TGT | CCT | CAG | TGC | AAA | ACT | CGA | TAC | AAA | AGG | TTA | AAA | GGT | AGT | CCA | CGG | | 520 |
| 35 | Cys | Pro | Gln | Сув | Lys | Thr | Arg | Tyr | Lys | Arg | Ile | Lys | Gly | Ser | Pro | Arg | | |
| | | | | | 85 | | | | | 90 | | | | | 95 | | | |
| | GTT | GAT | GGA | GAT | GAT | GAA | GAA | GAA | GAA | GAC | ATT | GAT | GAT | CTT | GAG | TAT | | 574 |
| | | | | Asp | | | | | | | | | | | | | | - 1 |
| 40 | | - | - | 100 | • | | | | 105 | - | | - | - | 110 | | - | | |

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| | GAG | TTT | GAT | CAT | GGG | ATG | GAC | CCT | GAA | CAT | GCC | GCT | GAA | GCC | GCA | CTC | 622 |
|----|-----|------|-------|---------|------------|---------|-----|---------|-----|------|-----|-------------|------|-----|---------|-------|------|
| | Glu | Phe | qeA | His | Gly | Met | Asp | Pro | Glu | His | Ala | Ala | Glu | Ala | Ala | Leu | |
| | | | 115 | | | | | 120 | | | | | 125 | | | | |
| | | | | | | | | | | | | | | | | | |
| 5 | TCT | TCA | CGC | CTT | AAC | ACC | GGT | CGT | GGT | GGA | TTG | GAT | TCA | GCT | CCA | CCT | 670 |
| | Ser | Ser | Arg | Leu | Asn | Thr | Gly | Arg | Gly | Gly | Leu | qeA | Ser | Ala | Pro | Pro | |
| | | 130 | | | | | 135 | | | | | 140 | | | | | |
| | | | | | | | | | | | | | | | | | |
| 10 | | | | | CCT | | | | | | | | | | | | 718 |
| 10 | | Ser | Gln | Ile | Pro | | Leu | Thr | Tyr | Cys | | Glu | Asp | Ala | Asp | | |
| | 145 | | | | | 150 | | | | | 155 | | | | | 160 | |
| | | mam | a.m | oom. | a.m | | omm | | ama | com | com | ma. | 100 | | | 000 | 7.5 |
| | | | | | CAT | | | | | | | | | | | | 766 |
| 15 | ıyı | 361 | nop | AIG | His | Ala | Deu | 116 | Vai | 170 | FIO | 261 | 1111 | GLY | 175 | Gly | |
| | | | | | 100 | | | | | ••• | | | | | 1.5 | | |
| | AAT | CGC | GTC | TAT | CCT | GCA | CCG | TTT | ACA | GAT | TCT | TCT | GCA | CCT | CCA | CAG | 814 |
| | | | | | Pro | | | | | | | | | | | | |
| | | _ | | 180 | | | | | 185 | - | | | | 190 | | | |
| 20 | | | | | | | | | | | | | | | | | |
| | GCG | AGA | TCA | ATG | GTT | CCT | CAG | AAA | GAT | ATT | GCG | GAA | TAT | GGT | TAT | GGA | 862 |
| | Ala | Arg | Ser | Met | Val | Pro | Gln | Lys | Asp | Ile | Ala | Glu | Tyr | Gly | Tyr | Gly | |
| | | | 195 | | | | | 200 | | | | | 205 | | | | |
| | | | | | | | | | | | | | | | | | |
| 25 | AGT | GTT | GCT | TGG | AAG | GAC | CGT | ATG | GAA | GTT | TGG | AAG | AGA | CGA | CAA | GGC | 910 |
| | Ser | Val | Ala | Trp | Lys | Asp | Arg | Met | Glu | Val | Trp | Lys | Arg | Arg | Gln | Gly | |
| | | 210 | | | | | 215 | | | | | 220 | | | | | |
| | | | | | | | | | | | | | | | | | |
| 30 | | | | | GTC | | | | | | | | | | | | 958 |
| 30 | | Lys | Leu | Gln | Val | | Lys | His | Glu | Gly | | | Asn | Gly | Arg | | |
| | 225 | | | | | 230 | | | | | 235 | | | | | 240 | |
| | maa | | | | | | ~~~ | | ~~= | | | | | | | 0 h m | |
| | | | | | GAC | | | | | | | | | | | | 1006 |
| 35 | Ser | ASII | Азр | дам | Авр 245 | GIU | Leu | Авр | Asp | | | mec | Pro | met | 255 | | |
| ,, | | | | | 443 | | | | | 250 | | | | | 433 | | |
| | GAA | GGA | AGA . | CAA | CCT | כדר | TCA | AGA | ЭАА | C-TA | CCT | ል ተጥ | Ссл | тса | AGO | AGA | 1054 |
| | | | | | Pro | | | | | | | | | | | | 2001 |
| | | 7 | 3 | 260 | | | | | 265 | | | | 5 | 270 | | | |
| | | | | | | | | | | | | | | | | | |

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| | ATA | TAA | CCT | TAC | AGG | ATG | TTA | TTA | CTG | TGT | CGC | CTC | GCG | TTA | CTT | GGT | 1102 |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
| | Ile | Asn | Pro | Tyr | Arg | Met | Leu | Ile | Leu | Сув | Arg | Leu | Ala | Ile | Leu | Gly | |
| | | | 275 | | | | | 280 | | | | | 285 | | | | |
| | | | | | | | | | | | | | | | | | |
| 5 | CTT | TTC | TTT | CAT | TAT | AGA | ATT | CTC | CAT | CCA | GTC | AAT | GAT | GCA | TAT | GGA | 1150 |
| | Leu | Phe | Phe | His | Tyr | Arg | Ile | Leu | His | Pro | Val | Asn | ĄsĄ | Ala | Tyr | Gly | |
| | | 290 | | | | | 295 | | | | | 300 | | | | | |
| | | | | | | | | | | | | | | | | | |
| | TTA | TGG | TTA | ACG | TCA | GTT | ATA | TGC | GAA | ATA | TGG | TTT | GCA | GTG | TCT | TGG | 1198 |
| 10 | Leu | Trp | Leu | Thr | Ser | Val | Ile | Cys | Glu | Ile | Trp | Phe | Ala | Val | Ser | Trp | |
| | 305 | | | | | 310 | | | | | 315 | | | | | 320 | |
| | | | | | | | | | | | | | | | | | |
| | ATT | CTT | GAT | CAA | TTC | CCC | AAA | TGG | TAT | CCT | ATA | GAA | CGT | GAA | ACA | TAC | 1246 |
| | Ile | Leu | qaA | Gln | Phe | Pro | Lys | Trp | Tyr | Pro | Ile | Glu | Arg | Glu | Thr | Tyr | |
| 15 | | | | | 325 | | | | | 330 | | | | | 335 | | |
| | | | | | | | | | | | | | | | | | |
| | CTC | GAT | AGA | CTC | TCT | CTC | AGG | TAC | GAG | AAG | GAA | GGA | AAA | CCG | TCA | GGA | 1294 |
| | Leu | Asp | Arg | Leu | Ser | Leu | Arg | Tyr | Glu | Lys | Glu | Gly | Lys | Pro | Ser | Gly | |
| | | | | 340 | | | | | 345 | | | | | 350 | | | |
| 20 | | | | | | | | | | | | | | | | | |
| | TTA | GCA | CCT | GTT | GAT | GTT | TTT | GTT | AGT | ACA | GTG | GAT | CCG | TTG | AAA | GAG | 1342 |
| | Leu | Ala | Pro | Val | Asp | Val | Phe | Val | Ser | Thr | Val | Asp | Pro | Leu | Lys | Glu | |
| | | | 355 | | | | | 360 | | | | | 365 | | | | |
| | | | | | | | | | | | | | | | | | |
| 25 | CCC | CCC | TTG | ATT | ACA | GCA | AAC | ACA | GTT | CTT | TCC | ATT | CTA | GCA | GTT | GAT | 1390 |
| | Pro | Pro | Leu | Ile | Thr | Ala | Asn | Thr | Val | Leu | Ser | Ile | Leu | Ala | Val | Asp | |
| | | 370 | | | | | 375 | | | | | 380 | | | | | |
| | | | | | | | | | | | | | | | | | |
| | TAT | CCT | GTG | GAT | AAG | GTT | GCG | TGT | TAT | GTA | TCA | AAC | AAT | GGT | GCA | GCT | 1438 |
| 30 | Tyr | Pro | Val | Asp | Lys | Val | Ala | Сув | Tyr | Val | Ser | Asn | Asn | Gly | Ala | Ala | |
| | 385 | | | | | 390 | | | | | 395 | | | | | 400 | |
| | | | | | | | | | | | | | | | | | |
| | ATG | CTT | ACA | TTT | GAA | GCT | CTC | TCT | GAT | ACA | GCT | GAT | TTT | GCT | ACA | AAA | 1486 |
| | Met | Leu | Thr | Phe | Glu | Ala | Leu | Ser | Asp | Thr | Ala | Asp | Phe | Ala | Thr | Lys | |
| 35 | | | | | 405 | | | | | 410 | | | | | 415 | | |
| | | | | | | | | | | | | | | | | | |
| | TGG | GTT | CCT | TTT | TGT | AAG | AAG | TTT | AAT | ATC | GAG | CCA | CGA | GCT | CCT | GAG | 1534 |
| | Trp | Val | Pro | Phe | Сув | Lys | Lya | Phe | Asn | Ile | Glu | Pro | Arg | Ala | Pro | Glu | |
| | | | | 420 | | | | | 425 | | | | | 430 | | | |

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| | TGG | TAT | TTT | TCT | CAG | AAG | ATG | GAT | TAC | CTG | AAG | AAC | AAA | GTT | CAT | CCT | 15 | 82 |
|----|------|-------|----------|-------------|--------|------|------|---------|--------|-----|-----|------|------------|------|-----------|------|----|-----|
| | Trp | Tyr | Phe | Ser | Gln | Lys | Met | Asp | Tyr | Leu | Lys | naA | Lys | Val | His | Pro | | |
| | | | 435 | | | | | 440 | | | | | 445 | | | | | |
| | | | | | | | | | | | | | | | | | | |
| 5 | GCT | TTT | GTC | AGG | GAA | CGT | CGT | GCT | ATG | AAG | AGA | GAT | TAT | GAA | GAG | TTT | 16 | 30 |
| | Ala | Phe | Val | Arg | Glu | Arg | Arg | Ala | Met | Lys | Arg | Asp | Tyr | Glu | Glu | Phe | | |
| | | 450 | | | | | 455 | | | | | 460 | | | | | | |
| | | | | | | | | | | | | | | | | | | |
| | AAA | GTG | AAG | ATA | AAT | GCA | CTG | GTT | GCT | ACT | GCA | CAG | AAA | GTG | CCT | GAG | 16 | 78 |
| 10 | Lys | Val | Lys | Ile | Asn | Ala | Leu | Val | Ala | Thr | Ala | Gln | Lys | Val | Pro | Glu | | |
| | 465 | | | | | 470 | | | | | 475 | | | | | 480 | | |
| | | | | | | | | | | | | | | | | | | |
| | GAA | CGT | TGG | ACT | ATG | CAA | GAT | GGA | ACT | CCT | TGG | CCT | GGA | AAC | AAC | GTC | 17 | 26 |
| | Glu | Arg | Trp | Thr | Met | Gln | Asp | Gly | Thr | Pro | Trp | Pro | Gly | Asn | Asn | Val | | |
| 15 | | | | | 485 | | | | | 490 | | | | | 495 | | | |
| | | | | | | | | | | | | | | | | | | |
| | CGT | GAC | CAT | CCT | GGA | ATG | ATT | CAG | GTG | TTC | TTG | GGT | CAT | AGT | GGA | GTT | 17 | 74 |
| | Arg | Asp | His | Pro | Gly | Met | Ile | Gln | | Phe | Leu | Gly | His | Ser | Gly | Val | | |
| 20 | | | | 500 | | | | | 505 | | | | | 510 | | | | |
| 20 | | | | | | | | | | | | | | | | | | |
| | CGT | GAT | ACG | GAT | GGT | AAT | GAG | TTA | CCA | CGT | CTA | GTG | TAT | GTT | TCT | CGT | 18 | 322 |
| | Arg | Asp | | Asp | Gly | Asn | Glu | | Pro | Arg | Leu | Val | • | Val | Ser | Arg | | |
| | | | 515 | | | | | 520 | | | | | 525 | | | | | |
| 25 | | | | | | | | | | | | | | | | | | |
| 23 | | | | | | | | | | | | GCT | | | | | 18 | 370 |
| | GIu | - | Arg | Pro | Gly | Phe | _ | His | His | Lys | Lys | Ala | Gly | Ala | Met | Asn | | |
| | | 530 | | | | | 535 | | | | | 540 | | | | | | |
| | maa | mmo | . | aa > | ama | mam | 0.00 | | Gm. | max | | 0.00 | | m> 0 | - Carrier | amm. | | |
| 30 | | | | | | | | | | | | GCT | | | | | 13 | 18 |
| 30 | | Leu | 116 | Arg | vaı | | ATS | vaı | rea | ser | | Ala | Pro | lyr | ьeu | | | |
| | 545 | | | | | 550 | | | | | 555 | | | | | 560 | | |
| | እስጥ | C TO | CAT | mor. | C N TT | CNC | ma c | N TO CO | 220 | 220 | 300 | | 003 | » mm | 202 | GAA | | |
| | | | | | | | | | | | | | | | | | 13 | 966 |
| 35 | ASII | vai | Авр | сув | _ | HIS | ıyı | 116 | ABN | | ser | Lys | Ala | ire | _ | GIU | | |
| " | | | | | 565 | | | | | 570 | | | | | 575 | | | |
| | ጥረማ | ክ ጥር | Trans. | THE CO | 7 m~ | 7 TV | CAC | ccc | C1 N N | TCC | cor | 770 | 777 | C mm | - mom | ጥእጥ | 2. | 114 |
| | | | | | | | | | | | | Lys | | | | TAT | 20 |)14 |
| | Jer | rie (| cys | | | riec | veb | FIO | | | GIÅ | пåя | nys | | - | 171 | | |
| | | | | 580 | | | | | 585 | | | | | 590 | | | | |

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| | GTT | CAG | TTT | CCG | CAG | AGA | TTT | GAT | GGG | ATT | GAT | AGA | CAT | GAT | AGA | TAC | 2062 |
|----|-----|------|-----|-----|------|------|---------|-----|-----|-----|------|------------|------------|-----|-----|--------------|------|
| | Val | Gln | Phe | Pro | Gln | Arg | Phe | Asp | Gly | Ile | Asp | Arg | His | qeA | Arg | Tyr | |
| | | | 595 | | | | | 600 | | | | | 605 | | | | |
| | | | | | | | | | | | | | | | | | |
| 5 | TCA | AAC | CGT | AAC | GTT | GTG | TTC | TTT | GAT | ATT | AAC | ATG | AAA | GGT | CTT | GAT | 2110 |
| | Ser | Asn | Arg | naA | Val | Val | Phe | Phe | Asp | Ile | Asn | Met | Lys | Gly | Leu | Asp | |
| | | 610 | | | | | 615 | | | | | 620 | | | | | |
| | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | TGT | | | | | 2158 |
| 10 | Gly | Ile | Gln | Gly | Pro | Ile | Tyr | Val | Gly | Thr | Gly | Сув | Val | Phe | Arg | Lys | |
| | 625 | | | | | 630 | | | | | 635 | | | | | 640 | |
| | | | | | | | | | | | | | | | | | |
| | CAG | GCT | CTT | TAT | GGT | TTT | GAT | GCA | CCA | AAG | AAG | AAG | AAA | CCA | CCA | GGC | 2206 |
| | Gln | Ala | Leu | Tyr | Gly | Phe | Asp | Ala | Pro | Lys | Lys | Lys | Lys | Pro | Pro | Gly | |
| 15 | | | | | 645 | | | | | 650 | | | | | 655 | | |
| | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | TTG | | | | | 2254 |
| | Lув | Thr | Сув | | Cys | Trp | Pro | Lys | - | Сув | Сув | Leu | Сув | - | Gly | Leu | |
| 20 | | | | 660 | | | | | 665 | | | | | 670 | | | |
| 20 | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | AAA | | | | | 2302 |
| | Arg | гуз | - | ser | ràs | Thr | гÀв | | Inr | Авр | rAs | Lys | | Asn | Inr | rys | |
| | | | 675 | | | | | 680 | | | | | 685 | | | | |
| 25 | CNC | 3 CT | TCN | 220 | CAC | አ ሙጣ | C 3 T | 000 | CTA | CAC | 220 | GTC | 636 | C | COT | C TOTAL | 2250 |
| 23 | | | | | | | | | | | | | | | | | 2350 |
| | GIU | 690 | ser | Буб | GIII | 116 | 695 | MIG | Dea | GIU | ASII | Val 700 | мsр | GIU | GIY | Val | |
| | | 030 | | | | | 0,5 | | | | | 700 | | | | | |
| | ATC | GTC | CCA | GTG | TCA | ТАА | ርም ጉ | GAG | DAA | AGA | TOT | GAA | GCA | ACA | CAA | ጥ ፕር፡ | 2398 |
| 30 | | | | | | | | | | | | Glu | | | | | |
| | 705 | | | | | 710 | | | -,- | 3 | 715 | | •••• | | | 720 | |
| | | | | | | | | | | | | | | | | | |
| | AAA | TTG | GAG | AAG | AAG | TTT | GGA | CAA | TCT | cca | GTT | TTC | GTT | GCC | тст | GCT | 2446 |
| | Lys | Leu | Glu | Lys | Lys | Phe | Gly | Gln | Ser | Pro | Val | Phe | Val | Ala | Ser | Ala | |
| 35 | • | | | • | 725 | | • | | | 730 | | | | | 735 | | |
| | | | | | | | | | | | | | | | · | | |
| | GTT | CTA | CAG | AAC | GGT | GGA | GTT | ccc | CGT | AAC | GCA | AGC | ccc | GCA | TGT | TTG | 2494 |
| | Val | Leu | Gln | Asn | Gly | Gly | Val | Pro | Arg | Asn | Ala | Ser | Pro | Ala | Сув | Leu | |
| | | | | 740 | | • | | | 745 | | | | | 750 | - | | |
| 40 | | | | | | | | | | | | | | | | | |

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| ATT | AGA | GAA | GCC | ATT | CAA | GTT | ATT | AGC | TGC | GGG | TAC | CAA | GAT | AAA | ACC | 2542 |
|------|---|--|--|--|---|---|--|--|--|---|---|--|---------|--------|--|--|
| Leu | Arg | Glu | Ala | Ile | Gln | Val | Ile | Ser | Cys | Gly | Tyr | Gln | Asp | Lys | Thr | |
| | | 755 | | | | | 760 | | | | | 765 | | | | |
| | | | | | | | | | | | | | | | | |
| GAA | TGG | GGA | AAA | GAG | ATC | GGG | TGG | ATT | TAT | GGA | TCG | GTG | ACT | GAA | GAT | 2590 |
| Glu | Trp | Gly | Lys | Glu | Ile | Gly | Trp | Ile | Tyr | Gly | Ser | Val | Thr | Glu | Asp | |
| | 770 | | | | | 775 | | | | | 780 | | | | | |
| | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | 2638 |
| Ile | Leu | Thr | Gly | Phe | Lys | Met | His | Сув | His | Gly | Trp | Arg | Ser | Val | Tyr | |
| 785 | | | | | 790 | | | | | 795 | | | | | 800 | |
| | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | 2686 |
| Cys | Met | Pro | Lys | Arg | Ala | Ala | Phe | Lys | Gly | Ser | Ala | Pro | Ile | Asn | Leu | |
| | | | | 805 | | | | | 810 | | | | | 815 | | |
| | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | 2734 |
| Ser | Asp | Arg | | His | Gln | Val | Leu | Arg | Trp | Ala | Leu | Gly | Ser | Val | Glu | |
| | | | 820 | | | | | 825 | | | | | 830 | | | |
| | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | 2782 |
| Ile | Phe | | Ser | Arg | His | Cys | | Ile | Trp | Tyr | Gly | Tyr | Gly | Gly | Gly | |
| | | 835 | | | | | 840 | | | | | 845 | | | | |
| | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | 2830 |
| Leu | | Trp | Leu | Glu | Arg | | Ser | Tyr | Ile | Asn | | Val | Val | Tyr | Pro | |
| | 850 | | | | | 855 | | | | | 860 | | | | | |
| mac. | 3. COM | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | 2878 |
| | inr | ser | Leu | PIO | | 116 | vai | lyr | Cys | | Leu | Pro | Ala | Val | | |
| 905 | | | | | 870 | | | | | 875 | | | | | 880 | |
| ጥጥአ | CT C | N C N | CON | | ጥጥረ | N.T.O. | CTC. | COM | CNC | 200 | 100 | | | | | |
| | | | | | | | | | | | | | | | | 2926 |
| Веч | Deu | 1111 | GIY | | FIIC | 116 | vai | PIO | | 116 | ser | ASN | lyr | | GIA | |
| | | | | 003 | | | | | 030 | | | | | 075 | | |
| ΔΤΔ | CTC | T TC | ልጥር | (-TC | מדת | ጥጥ | ልሞል | TCC | איזי אַ | CCD | Cur | እርጥ | COP | איירי | CTC C | 2974 |
| | | | | | | | | | | | | | | | | 23/4 |
| | | | | | | | | | 114 | n.u | 741 | 1.11 | - | 116 | nen. | |
| | | | | | | | | | | | | | 210 | | | |
| | GAA Glu ATC 11e 785 TGT Cys TCA Ser ATT 11e TTA Leu TGG Trp 865 TTA Leu ATA | Leu Arg GAA TGG Glu Trp 770 ATC CTG 11e Leu 785 TGA ATG Cys Met TCA GAT Ser Asp ATT TTC 11e Phe TTA AAA Leu Lys 850 TGG ACT Trp Thr 865 TTA CTC Leu Leu ATA CTC | Leu Arg Glu 755 GAA TGG GGA Glu Trp Gly 770 TGT ATG CCT Pro Met Pro TCA GAT CGT Pro Arg Arg TTA AAA TGG Leu Lys Trp 850 TGG ACT TCA Trp 850 TTA CTC ACA Trp Thr Ser 865 TTA CTC ACA Leu Leu Thr | Leu Arg Glu Ala GAA TGG GGA AAA Glu Trp Gly Lys ATC CTG ACG GGT TGT ATG CCT AAG CYs Met Pro Lys TCA GAT CGT CTT Ser Asp Arg Leu 820 Arg Leu ATT TTC TTG AGC Ile Phe Leu Ser 835 TTG Leu 850 TTP Leu 850 TCA CTT TTA CTC ACA GGA Leu EGT ACA GGA Leu Leu TTC ACA ATA CTC ACA GGA Leu Leu TTC ACA ATA CTC ACA ACA ATA CTC ACA </td <td>Leu Arg Glu Ala Gad GAA TGG GGA AAA GAG Glu Trp Gly Lys Glu ATC CTG ACG GGT TTC 11e Leu Thr Gly Phe 785 CCT AAG CGT CYS Met Pro Lys Arg 805 ATG CTT CAT Ser Asp Arg Leu His 820 AGA AL Phe Leu Ser Arg 835 TTG AGA AGA Leu Lys Trp Leu Glu 850 TTG CTC AGA THA ACA TCA CTT CCA TTA CTC ACA CTT CCA TTA CTC ACA CTT CCA TTA CTC ACA GGA AAA Leu Leu Pro Lys B85 ATA CTC ACA AGA AGA AAA Leu Leu TTC ACA AGA AAA Leu Leu TTC ATG CTC ATG ATG</td> <td>Leu Arg 755 Glu Ala 11e Gln 755 GAA 7GG GGA AAA GAG ATC Glu Trp 770 Lys Glu Ttc AAG 11e Leu Thr Gly Phe Lys 790 ATC CTG ACG GGT TTC AAG 11e Leu Thr Gly ATG ATG ATG ATG ATG ATG ATG ATG ATG ATG</td> <td>Leu Arg Glu Ala 11e Gln Val GAA TGG GGA AAA GAG ATC GGG Glu Trp Gly Lys Glu 11e Gly ATC CTG ACG GGT TTC AAG ATG TGI ATG CCT AAG CGT GCA GCT TGA ATG CTT CAT ALa Ala Ala TCA AGA AGG AGA CAT TGT ATT TTC TTG AGA AGA CAT TGT ATT TTC TTG AGA AGA AGA TTC TGT AGA AGA TTC TGT AGA AGA TTC TGT AGA AGA TTC AGA AGA TTC TTC AGA AGA TTC ATC TTC AGA AGA TTC ATC ATC TTC AG</td> <td>Heu Arg Glu Ala Ile Gln Val Ile 760 GAA TGG GGA AAA GAG ATC GGG TGG Glu Trp Gly Lys Glu Ile Gly Trp 770</td> <td>Leu Arg Glu Ala Ile Gln Val Ile Ser 760 GAA TGG GGA AAA GAG ATC GGG TGG ATT GIU TTP GIY Lys GIU Ile GIY TTP Ile ATC CTG ACG GGT TTC AAG ATG CAT TGC TGA ATG CCT AAG CGT GCA GCT TTA AAA CYS Met Pro Lys Arg Ala Ala Phe Lys TCA GAT CCT AAG CGT CAA GT CTA CAT Ser Asp Leu His Gln Val Leu Arg Ser Asp Arg Arg Arg CTA TGC ATA TTA AAA TGG ATG AGA ATC TCT TAC Leu</td> <td>Leu Arg Glu Ala Ile Gln Val Ile Ser Cys GAA TGG GGA AAA GAG ATC GGG TGG ATT TAT GIU Trp Gly Lys Glu Ile Gly Trp Ile Tyr ATC CTG GCT TTC AAG ATG ATG CAT TTT AAA GAT TGA ATG CCT AAG CGT GCA GCT TTT AAA GGA CYs Met Pro Lys Arg Ala Ala Phe Lys ATG TTG ATG ATG TTT ATG A</td> <td>Leu Arg Glu Ala Ile Gln Val Ile Ser Cys Gly GAA TGG GGA AAA GAG ATC GGG TGG ATT TAT GGA Glu Trp Gly Lys GGT TTC AAG GGT TTC AGG AGG TTT AAA GGY AGG AGG AGG AGG TTT AAA GGT AGG AGG</td> <td>Leu Arg Glu Ala Ile Gln Val Val 760 Ser Cys Gly Tyr 760 Tyr Cys Cys Gly Tyr 760 GAA TGG GGA AAA GAG GU Trp Gly Lys Glu Ile Gly Trp Gly Tyr 770 The Gly Trp Gly Tyr 770 The Gly Trp Gly Tyr 770 The Gly Trp 770 The Gly Trp 770 The Gly Trp 770 The Gly Trp 780 The Gly Trp 780</td> <td> Column</td> <td> Column</td> <td> Column C</td> <td>GAA TGG GGA AAA GAG ATC GGG TGG ATT TAT GGA TCG GTG ACT GAA GAT Glu Trp Gly Lys Glu Ile Gly Trp Ile Tyr Gly Ser Val Thr Glu Asp 770 775 780 ATC CTG ACG GGT TTC AAG ATG CAT TGC CAT GGA TGG AGA TCT GTG TAC Ile Leu Thr Gly Phe Lys Met His Cys His Gly Trp Arg Ser Val Tyr 785 790 795 800 TGT ATG CCT AAG CGT GCA GCT TTT AAA GGA TCT GCT CCT ATT AAC TTG Cys Met Pro Lys Arg Ala Ala Phe Lys Gly Ser Ala Pro Ile Asn Leu 805 810 815 TCA GAT CGT CTT CAT CAA GTT CTA CGT TGG GCT CTT GGC TCT GTA GAG Ser Asp Arg Leu His Gln Val Leu Arg Trp Ala Leu Gly Ser Val Glu 820 825 830 ATT TTC TTG AGC AGA CAT TGT CCG ATA TGG TAT GGT TAT GGT GGT Ile Phe Leu Ser Arg His Cys Pro Ile Trp Tyr Gly Tyr Gly Gly Gly 835 840 845 TTA AAA TGG TTG GAG AGA TTC TCT TAC ATC AAC TCT GTC GTC TAT CCT Leu Lys Trp Leu Glu Arg Phe Ser Tyr Ile Asn Ser Val Val Tyr Pro 850 855 850 860 TGG ACT TCA CTT CCA TTG ATC GTC TAT TGT TCT CCC GCG GTT TGT Trp Thr Ser Leu Pro Leu Ile Val Tyr Cys Ser Leu Pro Ala Val Cys 865 870 890 895 ATA CTC TTC ATG CTC ATG TTC ATA TCC ATA GGA GTA ACT GGA ATC CTC Ile Leu Phe Met Leu Met Phe Ile Ser Ile Ala Val Thr Gly Ile Leu</td> | Leu Arg Glu Ala Gad GAA TGG GGA AAA GAG Glu Trp Gly Lys Glu ATC CTG ACG GGT TTC 11e Leu Thr Gly Phe 785 CCT AAG CGT CYS Met Pro Lys Arg 805 ATG CTT CAT Ser Asp Arg Leu His 820 AGA AL Phe Leu Ser Arg 835 TTG AGA AGA Leu Lys Trp Leu Glu 850 TTG CTC AGA THA ACA TCA CTT CCA TTA CTC ACA CTT CCA TTA CTC ACA CTT CCA TTA CTC ACA GGA AAA Leu Leu Pro Lys B85 ATA CTC ACA AGA AGA AAA Leu Leu TTC ACA AGA AAA Leu Leu TTC ATG CTC ATG | Leu Arg 755 Glu Ala 11e Gln 755 GAA 7GG GGA AAA GAG ATC Glu Trp 770 Lys Glu Ttc AAG 11e Leu Thr Gly Phe Lys 790 ATC CTG ACG GGT TTC AAG 11e Leu Thr Gly ATG | Leu Arg Glu Ala 11e Gln Val GAA TGG GGA AAA GAG ATC GGG Glu Trp Gly Lys Glu 11e Gly ATC CTG ACG GGT TTC AAG ATG TGI ATG CCT AAG CGT GCA GCT TGA ATG CTT CAT ALa Ala Ala TCA AGA AGG AGA CAT TGT ATT TTC TTG AGA AGA CAT TGT ATT TTC TTG AGA AGA AGA TTC TGT AGA AGA TTC TGT AGA AGA TTC TGT AGA AGA TTC AGA AGA TTC TTC AGA AGA TTC ATC TTC AGA AGA TTC ATC ATC TTC AG | Heu Arg Glu Ala Ile Gln Val Ile 760 GAA TGG GGA AAA GAG ATC GGG TGG Glu Trp Gly Lys Glu Ile Gly Trp 770 | Leu Arg Glu Ala Ile Gln Val Ile Ser 760 GAA TGG GGA AAA GAG ATC GGG TGG ATT GIU TTP GIY Lys GIU Ile GIY TTP Ile ATC CTG ACG GGT TTC AAG ATG CAT TGC TGA ATG CCT AAG CGT GCA GCT TTA AAA CYS Met Pro Lys Arg Ala Ala Phe Lys TCA GAT CCT AAG CGT CAA GT CTA CAT Ser Asp Leu His Gln Val Leu Arg Ser Asp Arg Arg Arg CTA TGC ATA TTA AAA TGG ATG AGA ATC TCT TAC Leu | Leu Arg Glu Ala Ile Gln Val Ile Ser Cys GAA TGG GGA AAA GAG ATC GGG TGG ATT TAT GIU Trp Gly Lys Glu Ile Gly Trp Ile Tyr ATC CTG GCT TTC AAG ATG ATG CAT TTT AAA GAT TGA ATG CCT AAG CGT GCA GCT TTT AAA GGA CYs Met Pro Lys Arg Ala Ala Phe Lys ATG TTG ATG ATG TTT ATG A | Leu Arg Glu Ala Ile Gln Val Ile Ser Cys Gly GAA TGG GGA AAA GAG ATC GGG TGG ATT TAT GGA Glu Trp Gly Lys GGT TTC AAG GGT TTC AGG AGG TTT AAA GGY AGG AGG AGG AGG TTT AAA GGT AGG AGG | Leu Arg Glu Ala Ile Gln Val Val 760 Ser Cys Gly Tyr 760 Tyr Cys Cys Gly Tyr 760 GAA TGG GGA AAA GAG GU Trp Gly Lys Glu Ile Gly Trp Gly Tyr 770 The Gly Trp Gly Tyr 770 The Gly Trp Gly Tyr 770 The Gly Trp 770 The Gly Trp 770 The Gly Trp 770 The Gly Trp 780 The Gly Trp 780 | Column | Column | Column C | GAA TGG GGA AAA GAG ATC GGG TGG ATT TAT GGA TCG GTG ACT GAA GAT Glu Trp Gly Lys Glu Ile Gly Trp Ile Tyr Gly Ser Val Thr Glu Asp 770 775 780 ATC CTG ACG GGT TTC AAG ATG CAT TGC CAT GGA TGG AGA TCT GTG TAC Ile Leu Thr Gly Phe Lys Met His Cys His Gly Trp Arg Ser Val Tyr 785 790 795 800 TGT ATG CCT AAG CGT GCA GCT TTT AAA GGA TCT GCT CCT ATT AAC TTG Cys Met Pro Lys Arg Ala Ala Phe Lys Gly Ser Ala Pro Ile Asn Leu 805 810 815 TCA GAT CGT CTT CAT CAA GTT CTA CGT TGG GCT CTT GGC TCT GTA GAG Ser Asp Arg Leu His Gln Val Leu Arg Trp Ala Leu Gly Ser Val Glu 820 825 830 ATT TTC TTG AGC AGA CAT TGT CCG ATA TGG TAT GGT TAT GGT GGT Ile Phe Leu Ser Arg His Cys Pro Ile Trp Tyr Gly Tyr Gly Gly Gly 835 840 845 TTA AAA TGG TTG GAG AGA TTC TCT TAC ATC AAC TCT GTC GTC TAT CCT Leu Lys Trp Leu Glu Arg Phe Ser Tyr Ile Asn Ser Val Val Tyr Pro 850 855 850 860 TGG ACT TCA CTT CCA TTG ATC GTC TAT TGT TCT CCC GCG GTT TGT Trp Thr Ser Leu Pro Leu Ile Val Tyr Cys Ser Leu Pro Ala Val Cys 865 870 890 895 ATA CTC TTC ATG CTC ATG TTC ATA TCC ATA GGA GTA ACT GGA ATC CTC Ile Leu Phe Met Leu Met Phe Ile Ser Ile Ala Val Thr Gly Ile Leu |

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| | GAA | ATG | CAA | TGG | GGA | GGT | GTC | GGA | ATC | GAT | GAT | TGG | TGG | AGA | AAC | GAG | 3022 |
|-----|-----|------|-----|------|------|------|------|------|-----|-----|------|------|-----|------|------|------|------|
| | Glu | Met | Gln | Trp | Gly | Gly | Val | Gly | Ile | qaA | Asp | Trp | Trp | Arg | Asn | Glu | |
| | | | 915 | | | | | 920 | | | | | 925 | | | | |
| | | | | | | | | | | | | | | | | | |
| 5 | CAG | TTT | TGG | GTA | ATC | GGA | GGG | GCC | TCC | TCG | CAT | CTA | TTT | GCT | CTG | TTT | 3070 |
| | Gln | Phe | Trp | Val | Ile | Gly | Gly | Ala | Ser | Ser | His | Leu | Phe | Ala | Leu | Phe | |
| | | 930 | | | | | 935 | | | | | 940 | | | | | |
| | | | | | | | | | | | | | | | | | |
| | CAA | GGT | TTG | CTC | AAA | GTT | CTA | GCC | GGA | GTT | AAC | ACG | AAT | TTC | ACA | GTC | 3118 |
| 10 | Gln | Gly | Leu | Leu | Lys | Val | Leu | Ala | Gly | Val | Asn | Thr | Asn | Phe | Thr | Val | |
| | 945 | | | | | 950 | | | | | 955 | | | | | 960 | |
| | | | | | | | | | | | | | | | | | |
| | ACT | TCA | AAA | GCA | GCA | GAC | GAT | GGA | GCT | TTC | TCT | GAG | CTT | TAC | ATC | TTC | 3166 |
| | Thr | Ser | Lys | Ala | Ala | Asp | Asp | Gly | Ala | Phe | Ser | Glu | Leu | Tyr | Ile | Phe | |
| 15 | | | | | 965 | | | | | 970 | | | | | 975 | | |
| | | | | | | | | | | | | | | | | | |
| | AAG | TGG | ACA | ACT | TTG | TTG | ATT | CCT | CCG | ACA | ACA | CTT | CTG | ATC | ATT | AAC | 3214 |
| | Lys | Trp | Thr | Thr | Leu | Leu | Ile | Pro | Pro | Thr | Thr | Leu | Leu | Ile | Ile | Asn | |
| | | | | 980 | | | | | 985 | | | | | 990 | | | |
| 20 | | | | | | | | | | | | | | | | | |
| | ATC | ATT | GGA | GTT | ATT | GTC | GGC | GTT | TCT | GAT | GCC | ATT | AGC | TAA | GGC | TAT | 3262 |
| | Ile | Ile | Gly | Val | Ile | Val | Gly | Val | Ser | Asp | Ala | Ile | Ser | Asn | Gly | Tyr | |
| | | | 995 | | | | | 1000 |) | | | | 100 | 5 | | | |
| | | | | | | | | | | | | | | | | | |
| 25 | GAC | TCA | TGG | GGA | CCT | CTC | TTT | GGG | AGA | CTT | TTC | TTC | GCT | CTT | TGG | GTC | 3310 |
| | Asp | Ser | Trp | Gly | Pro | Leu | Phe | Gly | Arg | Leu | Phe | Phe | Ala | Leu | Trp | Val | |
| | | 1010 |) | | | | 1015 | 5 | | | | 1026 |) | | | | |
| | | | | | | | | | | | | | | | | | |
| • • | | | CAT | | | | | | | | | | | | | | 3358 |
| 30 | Ile | Val | His | Leu | Tyr | Pro | Phe | Leu | Lys | Gly | Met | Leu | Gly | Lys | Gln | Asp | |
| | 102 | 5 | | | | 1030 | 0 | | | | 1039 | 5 | | | | 1040 | |
| | | | | | | | | | | | | | | | | | |
| | AAA | ATG | CCT | ACG | ATT | ATT | GTG | GTC | TGG | TCT | TTA | CTT | CTA | GCT | TCG | ATC | 3406 |
| | Lys | Met | Pro | Thr | Ile | lle | Val | Val | Trp | Ser | Ile | Leu | Leu | Ala | Ser | Ile | |
| 35 | | | | | 1049 | 5 | | | | 105 |) | | | | 1059 | 5 | |
| | | | | | | | | | | | | | | | | | |
| | TTG | ACA | CTC | TTG | TGG | GTC | AGA | ATT | AAC | CCG | TTT | GTG | GCT | AAA | GGG | GGA | 3454 |
| | Leu | Thr | Leu | Leu | Trp | Val | Arg | Ile | Asn | Pro | Phe | Val | Ala | Lys | Gly | Gly | |
| | | | | 1060 |) | | | | 106 | 5 | | | | 1070 |) | | |

| 11/O 00/00#40 | DOM: 4 107/00403 |
|---------------|------------------|
| WO 98/00549 | PCT/AU97/00402 |

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| | CCA GTG TTG GAG ATC TGT GGT CTG AAT TGT GGA AAC TAAGATCCTC | 3500 |
|----|--|------|
| | Pro Val Leu Glu Ile Cys Gly Leu Asn Cys Gly Asn | |
| | 1075 1080 | |
| | | |
| 5 | AGTGAAAGAA GAGCAAAGGA GTTTGTGTTG GAGCTTTGGA AGCAAATGTG TTGATGATGA | 3560 |
| • | The second secon | 3300 |
| | TOCAN CHICAGO THE CHARLES ON A SACRECTICAL CHICAGO CHICAGO CHICAGO CON CHICAGO | |
| | TGCAAGTGTG TTTGTAGACA AAGATGTGCA GTTTTTACTT TTTACGACTT GTTAAACCTT | 3620 |
| | | |
| | TTTTGTTACC CCTAAATTAA TTCTTTTGTT ATCATGGTTA TACTAATAGA ATTGTTTGTT | 3680 |
| 10 | | |
| | TTTCTTTTTT ACATGTACTT TTAGTTATTC CGTAGTTATT GTATAATACT GATAACGATC | 3740 |
| | | |
| | ATATATACAC ACTITGITAA CAAAAAAAAA AAAAAAAAAA AAAAAAAAA AAAGCGGCCG | 3800 |
| | | |
| 15 | CTCGAATTGT CGACGCGGCC GCGAATTC | 3828 |
| | | 3020 |
| | | |
| | | |
| | | |
| | | |
| 20 | (2) INFORMATION FOR SEQ ID NO:8: | |
| | | |
| | (i) SEQUENCE CHARACTERISTICS: | |
| | (A) LENGTH: 1084 amino acids | |
| | (B) TYPE: amino acid | |
| 25 | (D) TOPOLOGY: linear | |
| | (b) Toroboot. Timeat | |
| | | |
| | (ii) MOLECULE TYPE: protein | |
| | | |
| | (xi) SEQUENCE DESCRIPTION: SEQ ID NO:8: | |
| 30 | | |
| | Met Asn Thr Gly Gly Arg Leu Ile Ala Gly Ser His Asn Arg Asn Glu | |
| | 1 5 10 15 | |
| | | |
| | Phe Val Leu Ile Asn Ala Asp Glu Ser Ala Arg Ile Arg Ser Val Gln | |
| 35 | · · · · · · · · · · · · · · · · · · · | |
| رر | 20 25 30 | |
| | | |
| | Glu Leu Ser Gly Gln Thr Cys Gln Ile Cys Gly Asp Glu Ile Glu Leu | |
| | 35 40 45 | |

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Thr Val Ser Ser Glu Leu Phe Val Ala Cys Asn Glu Cys Ala Phe Pro

| | | 50 | | | | | 55 | | | | | 60 | | | | |
|----|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|-----------------|
| 5 | Val 65 | Cys | Arg | Pro | Сув | Туг 70 | Glu | Туr | Glu | Arg | Arg 75 | Glu | Gly | Asn | Gln | A1: |
| | Сув | Pro | Gln | Cys | Lys 85 | Thr | Arg | Tyr | Lys | Arg 90 | Ile | Lys | Gly | Ser | Pro 95 | Arg |
| 10 | Val | Asp | Gly | Asp | Asp | Glu | Glu | Glu | Glu 105 | Asp | Ile | Asp | Asp | Leu 110 | Glu | Ту |
| 15 | Glu | Phe | Asp 115 | His | Gly | Met | Asp | Pro 120 | Glu | His | Ala | Ala | Glu 125 | Ala | Ala | Lei |
| 13 | Ser | Ser | Arg | Leu | Asn | Thr | Gly 135 | Arg | Gly | Gly | Leu | Asp 140 | Ser | Ala | Pro | Pro |
| 20 | Gly 145 | Ser | Gln | Ile | Pro | Leu 150 | Leu | Thr | Tyr | Сув | Авр 155 | Glu | Asp | Ala | Азр | Me: |
| | Tyr | Ser | Asp | Arg | His 165 | Ala | Leu | Ile | Val | Pro 170 | Pro | Ser | Thr | Gly | Tyr 175 | Gly |
| 25 | Asn | Arg | Val | Tyr 180 | Pro | Ala | Pro | Phe | Thr 185 | qsA | Ser | Ser | Ala | Pro 190 | Pro | Gli |
| 30 | Ala | Arg | Ser 195 | Met | Val | Pro | Gln | Lys 200 | Asp | Ile | Ala | Glu | Туг 205 | Gly | Tyr | Gly |
| | Ser | Val 210 | Ala | Trp | Lys | Asp | Arg 215 | Met | Glu | Val | Trp | Lys 220 | Arg | Arg | Gln | Gly |
| 35 | Glu 225 | Lys | Leu | Gln | Val | Ile 230 | Lys | His | Glu | Gly | Gly 235 | Asn | Asn | Gly | Arg | Gl ₃ |
| | Ser | Asn | Asp | Asp | Asp 245 | Glu | Leu | Asp | Asp | Pro 250 | Asp | Met | Pro | Met | Met 255 | Ası |

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| | Glu | Gly | Arg | Gln 260 | Pro | Leu | Ser | Arg | Lys 265 | Leu | Pro | Ile | Arg | Ser 270 | Ser | Arg |
|----|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| 5 | Ile | Asn | Pro 275 | Tyr | Arg | Met | Leu | Ile 280 | Leu | Cys | Arg | Leu | Ala 285 | Ile | Leu | Gly |
| | Leu | Phe 290 | Phe | His | туг | Arg | Ile 295 | Leu | His | Pro | Val | Asn 300 | Asp | Ala | Tyr | Gly |
| 10 | Leu 305 | Trp | Leu | Thr | Ser | Val 310 | Ile | Сув | Glu | Ile | Trp 315 | Phe | Ala | Val | Ser | Trp 320 |
| 15 | Ile | Leu | Asp | Gln | Phe 325 | Pro | Lys | Trp | Tyr | Pro 330 | lle | Glu | Arg | Glu | Thr 335 | Tyr |
| 13 | Leu | Asp | Arg | Leu 340 | Ser | Leu | Arg | Tyr | Glu 345 | Lys | Glu | Gly | Lys | Pro 350 | Ser | Gly |
| 20 | Leu | Ala | Pro 355 | Val | Asp | Val | Phe | Val 360 | Ser | Thr | Val | Asp | Pro 365 | Leu | Lys | Glu |
| | Pro | Pro 370 | Leu | Ile | Thr | Ala | Asn 375 | Thr | Val | Leu | Ser | Ile 380 | Leu | Ala | Val | Asp |
| 25 | Туг 385 | Pro | Val | Asp | Lys | Val 390 | Ala | Сув | тут | Val | Ser 395 | Asn | Asn | Gly | Ala | Ala 400 |
| 10 | Met | Leu | Thr | Phe | Glu 405 | Ala | Leu | Ser | Asp | Thr 410 | Ala | Asp | Phe | Ala | Thr 415 | Lys |
| 30 | Trp | Val | Pro | Phe 420 | Сув | Lys | Lys | Phe | Asn 425 | Ile | Glu | Pro | Arg | Ala 430 | Pro | Glu |
| 35 | Trp | Tyr | Phe | Ser | Gln | Lys | Met | Asp 440 | Tyr | Leu | Lys | Asn | Lys 445 | Val | His | Pro |
| | Ala | Phe 450 | Val | Arg | Glu | Arg | Arg 455 | Ala | Met | Lys | Arg | Asp 460 | туг | Glu | Glu | Phe |

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| | Lys 465 | | . Lys | Ile | Asn | Ala 470 | Leu | Val | Ala | Thr | Ala 475 | Gln | Lys | Val | Pro | G1: |
|----|------------|-------|------------|------------|------------|------------|------------|------------|------------|-------------------|------------|------------|------------|------------|------------|-------------|
| | G1: | ı Arg | Trp | Thr | Met 485 | Gln | Asp | Gly | Thr | Pro 490 | Trp | Pro | Gly | Asn | Asn 495 | Va] |
| | Arg | , Asp | His | Pro 500 | Gly | Met | Ile | Gln | Val 505 | Phe | Leu | Gly | Hıs | Ser 510 | Gly | Va] |
| 10 | O Arg | , Asp | Thr 515 | | Gly | Asn | Glu | Leu 520 | Pro | Arg | Leu | Val | Tyr 525 | Val | Ser | Arg |
| 1. | | 530 | Arg | Pro | Gly | Phe | Asp 535 | His | His | Lys | Lys | Ala 540 | Gly | Ala | Met | Asr |
| 13 | | | lle | Arg | Val | Ser 550 | Ala | Val | Leu | Ser | Asn 555 | Ala | Pro | Tyr | Leu | Le v |
| 20 | | ı Val | Asp | Сув | Asp 565 | His | Tyr | Ile | Asn | Asn 570 | Ser | Lys | Ala | Ile | Arg 575 | Glu |
| | Ser | : Met | Cys | Phe 580 | Met | Met | Asp | Pro | Gln 585 | Ser | Gly | Lys | Lys | Val 590 | Сув | Туг |
| 25 | 5 val | . Gln | Phe 595 | Pro | Gln | Arg | Phe | Asp | Gly | Ile | Asp | Arg | His 605 | Asp | Arg | Туг |
| 30 | | 610 | Arg | Asn | Val | Val | Phe 615 | Phe | Asp | Ile | Asn | Met 620 | Lys | Gly | Leu | Asp |
| , | | | Gln | Gly | Pro | 11e 630 | Tyr | Val | Gly | Thr | Gly 635 | Сув | Val | Phe | Arg | Lys |
| 35 | | Ala | Leu | Tyr | Gly 645 | Phe | Asp | Ala | Pro | Lya 650 | Lys | Lys | Lys | Pro | Pro 655 | Gly |
| | Lys | Thr | Cys | Asn 660 | Cys | Trp | Pro | Lys | Trp 665 | Cys | Сув | Leu | Сув | Сув 670 | Gly | Leu |

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| | Arg | Lys | Lys | Ser | Lys | Thr | Lys | Ala | Thr | Asp | Lys | Lys | Thr | Asn | Thr | Lys |
|----|-----|----------|-----------|-----|-----|-----------|-----|---|-----|-----|------|-----|-----|-----|------------|-----|
| | | | 675 | | | | | 680 | | | | | 685 | | | |
| | | | | | | | | | | | | | | | | |
| _ | Glu | | Ser | Lys | Gln | Ile | | Ala | Leu | Glu | Asn | Val | Asp | Glu | Gly | Val |
| 5 | | 690 | | | | | 695 | | | | | 700 | | | | |
| | | | _ | | | | | | | | | | | | | |
| | | Val | Pro | Val | Ser | | Val | Glu | Lys | Arg | | Glu | Ala | Thr | Gln | |
| | 705 | | | | | 710 | | | | | 715 | | | | | 720 |
| 10 | • | • | 61 | • | • | D | ~ > | ~1 | | _ | | _, | | | _ | |
| 10 | Lys | Leu | GIU | гàв | | Pne | GIY | GIN | ser | | vai | Phe | Val | Ala | | Ala |
| | | | | | 725 | | | | | 730 | | | | | 735 | |
| | Val | Leu | Gln | Asn | Gly | G) v | Val | Pro | Ara | Asn | Δla | Ser | Pro | Δla | Cve | Len |
| | | | | 740 | 01, | 0-, | | | 745 | | | 501 | | 750 | -73 | bcu |
| 15 | | | | | | | | | | | | | | | | |
| | Leu | Arg | Glu | Ala | Ile | Gln | Val | Ile | Ser | Сув | Gly | Tyr | Gln | Дар | Lys | Thr |
| | | _ | 755 | | | | | 760 | | • | - | - | 765 | - | - | |
| | | | | | | | | | | | | | | | | |
| | Glu | Trp | Gly | Lys | Glu | Ile | Gly | Trp | Ile | Tyr | Gly | Ser | Val | Thr | Glu | qaA |
| 20 | | 770 | | | | | 775 | | | | | 780 | | | | |
| | | | | | | | | | | | | | | | | |
| | Ile | Leu | Thr | Gly | Phe | Lys | Met | His | Сув | His | Gly | Trp | Arg | Ser | Val | Tyr |
| | 785 | | | | | 790 | | | | | 795 | | | | | 800 |
| 25 | | | | | | | | | | | | | | | | |
| 23 | Сув | Met | Pro | ГÀв | | Ala | Ala | Phe | Lys | | Ser | Ala | Pro | Ile | | Leu |
| | | | | | 805 | | | | | 810 | | | | | 815 | |
| | C | . | . | • | *** | 01 | | • | | | | _ | ~\ | _ | | |
| | ser | Asp | Arg | 820 | Hıs | GIN | vai | Leu | | Trp | Ala | Leu | GIÀ | | Val | Glu |
| 30 | | | | 020 | | | | | 825 | | | | | 830 | | |
| | Ile | Phe | Leu | Ser | Arg | Hig | Cva | Pro | Tle | Trn | Tree | Glv | Tur | Gly | Glv | Glv |
| | | | 835 | | | | 0,0 | 840 | 110 | p | .,. | Gry | 845 | Gry | Oly | GIY |
| | | | | | | | | • | | | | | 0.5 | | | |
| | Leu | Lys | Trp | Leu | Glu | Arg | Phe | Ser | Tyr | Ile | Asn | Ser | Val | Val | Tyr | Pro |
| 35 | | 850 | - | | | • | 855 | | • | | | 860 | | | | |
| | | | | | | | | | | | | | | | | |
| | Trp | Thr | Ser | Leu | Pro | Leu | Ile | Val | Tyr | Cys | Ser | Leu | Pro | Ala | Val | Сув |
| | 865 | | | | | 870 | | | | | 875 | | | | | 880 |

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| | Leu | Leu | Thr | Gly | Lys 885 | Phe | Ile | Val | Pro | Glu 890 | Ile | Ser | Asn | Tyr | Ala 895 | Gly |
|----|-------------|------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|------------|------------|-------------|-------------|-------------|
| 5 | Ile | Leu | Phe | Met 900 | Leu | Met | Phe | Ile | Ser 905 | Ile | Ala | Val | Thr | Gly 910 | Ile | Leu |
| | Glu | Met | Gln 915 | ттр | Gly | Gly | Val | Gly 920 | Ile | Asp | Asp | Trp | Trp 925 | Arg | Asn | Glu |
| 10 | Gln | Phe 930 | Trp | Val | Ile | Gly | Gly 935 | Ala | Ser | Ser | His | Leu 940 | Phe | Ala | Leu | Phe |
| 15 | Gln 945 | Gly | Leu | Leu | Lys | Val 950 | Leu | Ala | Gly | Val | Asn 955 | Thr | Asn | Phe | Thr | Val 960 |
| 13 | Thr | Ser | Lys | Ala | Ala 965 | Asp | Азр | Gly | Ala | Phe 970 | Ser | Glu | Leu | Tyr | Ile 975 | Phe |
| 20 | Lys | Trp | Thr | Thr 980 | Leu | Leu | Ile | Pro | Pro 985 | Thr | Thr | Leu | Leu | Ile 990 | Ile | Asn |
| | Ile | Ile | Gly 995 | Val | Ile | Val | Gly | Val | | Asp | Ala | Ile | Ser 100 | | Gly | Tyr |
| 25 | Asp | Ser | | Gly | Pro | Leu | Phe 1019 | | Arg | Leu | Phe | Phe | | Leu | Trp | Val |
| 30 | Ile 1025 | | His | Leu | Tyr | Pro 1030 | | Leu | Lys | Gly | Met 1035 | | Gly | Lys | Gln | Asp 1040 |
| | Lys | Met | Pro | Thr | Ile 1045 | | Val | Val | Trp | Ser 1050 | | Leu | Leu | Ala | Ser 1055 | |
| 35 | Leu | Thr | Leu | Leu 1060 | | Val | Arg | Ile | Asn 1065 | Pro | Phe | Val | Ala | Lys 1070 | | Gly |
| | Pro | Val | Leu 1075 | | Ile | Сув | Gly | Leu 1080 | | Сув | Gly | Asn | | | | |

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(2) INFORMATION FOR SEQ ID NO:9:

| | (i) : | SEQUENCE CHARACTERISTICS: | |
|----|-----------|---|-----|
| | | (A) LENGTH: 3614 base pairs | |
| 5 | | (B) TYPE: nucleic acid | |
| | | (C) STRANDEDNESS: single | |
| | | (D) TOPOLOGY: linear | |
| | | | |
| | (ii) | MOLECULE TYPE: cDNA | |
| 10 | | | |
| | (iii) | HYPOTHETICAL: NO | |
| | | | |
| | (vi) | ORIGINAL SOURCE: | |
| | | (A) ORGANISM: Arabidopsis thaliana | |
| 15 | | (B) STRAIN: Columbia | |
| | 4 | | |
| | (V11) | IMMEDIATE SOURCE: | |
| | | (B) CLONE: Ath-B | |
| 20 | (ix) | FEATURE: | |
| | (200) | (A) NAME/KEY: CDS | |
| | | (B) LOCATION: 2173411 | |
| | | (a) | |
| | | | |
| 25 | (xi) | SEQUENCE DESCRIPTION: SEQ ID NO:9: | |
| | | | |
| | GAATTCGCG | G CCGCGTCGAC TACGGCTGCG AGAAGACGAC AGAAGGGGGAT CCCAAGATTC | 60 |
| | | | |
| | TCCTCTTCG | ET CTTCCTTATA AACTATCTCT CTGTAGAGAA GAAAGCTTGG ATCCAGATTG | 120 |
| 30 | | | |
| | AGAGAGATT | TC AGAGAGCCAC ATCACCACAC TCCATCTTCA GATCTCATGA TTTGAACTAT | 180 |
| | | | |
| | TCCGACGTT | TT CGGTGTTGGA AGCAACTAAG TGACAA ATG GAA TCC GAA GGA GAA | 234 |
| | | Met Glu Ser Glu Gly Glu | |
| 35 | | 1 5 | |
| | | | |
| | | GGA AAG CCG ATG AAG AAC ATT GTT CCG CAG ACT TGC CAG ATC | 282 |
| | TNY ALA G | Bly Lys Pro Met Lys Asn Ile Val Pro Gln Thr Cys Gln Ile | |
| 40 | | 10 15 20 | |
| ¬υ | | | |

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| | TGT | AGT | GAC | AAT | GTT | GGC | AAG | ACT | GTT | GAT | GGA | GAT | CGT | TTT | GTG | GCT | 330 |
|----|------|-----|--------|-----|-----|-----------|-----|------|-----|------|-------------|-----|------|-----|------|-----|-----|
| | Cys | Ser | Asp | Asn | Val | Gly | Lys | Thr | Val | Авр | Gly | Asp | Arg | Phe | Val | Ala | |
| | | | 25 | | | | | 30 | | | | | 35 | | | | |
| _ | | | | | | | | | | | | | | | | | |
| 5 | | | | | | TTC | | | | | | | | | | | 378 |
| | Сув | - | Ile | Cys | Ser | Phe | | Val | Cys | Arg | Pro | _ | Tyr | Glu | Tyr | Glu | |
| | | 40 | | | | | 45 | | | | | 50 | | | | | |
| | 3.00 | | C B TD | 000 | አክጥ | CAA | mom | mar. | | CNC | 7 00 | | 200 | 202 | m> c | *** | 425 |
| 10 | | | | | | Gln | | | | | | | | | | | 426 |
| 10 | 55 | цуз | veħ | GIY | nan | 60 | 261 | Cys | FIO | GIII | 65 | Був | 1111 | Arg | ıyı | 70 | |
| | 33 | | | | | 00 | | | | | 95 | | | | | 70 | |
| | AGG | CTC | AAA | GGT | AGT | ССТ | GCT | ATT | CCT | GGT | GAT | AAA | GAC | GAG | GAT | GGC | 474 |
| | | | | | | Pro | | | | | | | | | | | |
| 15 | J | | • | • | 75 | | | | | 80 | • | • | • | | 85 | • | |
| | | | | | | | | | | | | | | | | | |
| | TTA | GCT | GAT | GAA | GGT | ACT | GTT | GAG | TTC | AAC | TAC | CCT | CAG | AAG | GAG | AAA | 522 |
| | Leu | Ala | Asp | Glu | Gly | Thr | Val | Glu | Phe | Asn | Tyr | Pro | Gln | Lys | Glu | Lys | |
| | | | | 90 | | | | | 95 | | | | | 100 | | | |
| 20 | | | | | | | | | | | | | | | | | |
| | ATT | TCA | GAG | CGG | ATG | CTT | GGT | TGG | CAT | CTT | ACT | CGT | GGG | AAG | GGA | GAG | 570 |
| | Ile | Ser | Glu | Arg | Met | Leu | Gly | Trp | His | Leu | Thr | Arg | Gly | Lys | Gly | Glu | |
| | | | 105 | | | | | 110 | | | | | 115 | | | | |
| | | | | | | | | | | | | | | | | | |
| 25 | GAA | ATG | GGG | GAA | CCC | CAG | TAT | GAT | AAA | GAG | GTC | TCT | CAC | AAT | CAT | CTT | 618 |
| | Glu | Met | Gly | Glu | Pro | Gln | Tyr | Asp | Lys | Glu | Val | Ser | His | naA | His | Leu | |
| | | 120 | | | | | 125 | | | | | 130 | | | | | |
| | | | | | | | | | | | | | | | | | |
| 30 | | | | | | AGA | | | | | | | | | | | 666 |
| 50 | | Arg | Leu | Inr | ser | Arg | GIN | Asp | Thr | Ser | | GIU | Pne | Ser | Ala | | |
| | 135 | | | | | 140 | | | | | 145 | | | | | 150 | |
| | TCA | ССТ | GAA | CGC | CTC | тст | ата | тст | ጥርጥ | אריד | ATC | сст | GGG | CGA | ממ | CGC | 714 |
| | | | | | | Ser | | | | | | | | | | | /14 |
| 35 | | | | | 155 | - | | | | 160 | | | , | ; | 165 | | |
| | | | | | | | | | | | | | | | | | |
| | CTT | CCC | TAT | TCA | TCA | GAT | GTC | AAT | CAA | TCA | CCA | AAT | AGA | AGG | ATT | GTG | 762 |
| | Leu | Pro | Tyr | Ser | Ser | Asp | Val | Asn | Gln | Ser | Pro | Asn | Arg | Arg | Ile | Val | |
| | | | | 170 | | | | | 175 | | | | | 180 | | | |
| 40 | | | | | | | | | | | | | | | | | |

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| | GAT | CCT | GTT | GGA | CTC | GGG | AAT | GTA | GCT | TGG | AAG | GAG | AGA | GTT | GAT | GGC | 810 |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
| | Asp | Pro | Val | Gly | Leu | Gly | Asn | Val | Ala | Trp | Lys | Glu | Arg | Val | Asp | Gly | |
| | | | 185 | | | | | 190 | | | | | 195 | | | | |
| | | | | | | | | | | | | | | | | | |
| 5 | TGG | AAA | ATG | AAG | CAA | GAG | AAG | AAT | ACT | GGT | CCT | GTC | AGC | ACG | CAG | GCT | 858 |
| | Trp | Lys | Met | Lys | Gln | Glu | Lys | Asn | Thr | Gly | Pro | Val | Ser | Thr | Gln | Ala | |
| | | 200 | | | | | 205 | | | | | 210 | | | | | |
| | | | | | | | | | | | | | | | | | |
| | GCT | TCT | GAA | AGA | GGT | GGA | GTA | GAT | ATT | GAT | GCC | AGC | ACA | GAT | ATC | CTA | 906 |
| 10 | Ala | Ser | Glu | Arg | Gly | Gly | Val | Asp | Ile | Asp | Ala | Ser | Thr | Asp | Ile | Leu | |
| | 215 | | | | | 220 | | | | | 225 | | | | | 230 | |
| | | | | | | | | | | | | | | | | | |
| | GCA | GAT | GAG | GCT | CTG | CTG | AAT | GAC | GAA | GCG | AGG | CAG | CTT | CTG | TCA | AGG | 954 |
| | Ala | Asp | Glu | Ala | Leu | Leu | Asn | Asp | Glu | Ala | Arg | Gln | Leu | Leu | Ser | Arg | |
| 15 | | | | | 235 | | | | | 240 | | | | | 245 | | |
| | | | | | | | | | | | | | | | | | |
| | AAA | GTT | TCA | ATT | CCT | TCA | TCA | CGG | ATC | AAT | CCT | TAC | AGA | ATG | GTT | TTA | 1002 |
| | Lys | Val | Ser | Ile | Pro | Ser | Ser | Arg | Ile | Asn | Pro | Tyr | Arg | Met | Val | Ile | |
| | | | | 250 | | | | | 255 | | | | | 260 | | | |
| 20 | | | | | | | | | | | | | | | | | |
| | ATG | CTG | CGG | CTT | GTT | ATC | CTT | TGT | CTC | TTC | TTG | CAT | TAC | CGT | ATA | ACA | 1050 |
| | Met | Leu | Arg | Leu | Val | Ile | Leu | Сув | Leu | Phe | Leu | His | Tyr | Arg | Ile | Thr | |
| | | | 265 | | | | | 270 | | | | | 275 | | | | |
| | | | | | | | | | | | | | | | | | |
| 25 | AAC | CCA | GTG | CCA | AAT | GCC | TTT | GCT | CTA | TGG | CTG | GTC | TCT | GTG | ATA | TGT | 1098 |
| | Asn | Pro | Val | Pro | Asn | Ala | Phe | Ala | Leu | Trp | Leu | Val | Ser | Val | Ile | Сув | |
| | | 280 | | | | | 285 | | | | | 290 | | | | | |
| | | | | | | | | | | | | | | | | | |
| | GAG | ATC | TGG | TTT | GCC | TTA | TCC | TGG | ATT | TTG | GAT | CAG | TTT | CCC | AAG | TGG | 1146 |
| 30 | Glu | Ile | Trp | Phe | Ala | Leu | Ser | Trp | Ile | Leu | Asp | Gln | Phe | Pro | Lys | Trp | |
| | 295 | | | | | 300 | | | | | 305 | | | | | 310 | |
| | | | | | | | | | | | | | | | | | |
| | TTT | CCT | GTG | AAC | CGT | GAA | ACC | TAC | CTC | GAC | AGG | CTT | GCT | TTA | AGA | TAT | 1194 |
| | Phe | Pro | Val | Asn | Arg | Glu | Thr | Tyr | Leu | Asp | Arg | Leu | Ala | Leu | Arg | Tyr | |
| 35 | | | | | 315 | | | | | 320 | | | | | 325 | | |
| | | | | | | | | | | | | | | | | | |
| | GAT | CGT | GAA | GGT | GAG | CCA | TCA | CAG | TTA | GCT | GCT | GTT | GAC | ATT | TTC | GTG | 1242 |
| | Asp | Arg | Glu | Gly | Glu | Pro | Ser | Gln | Leu | Ala | Ala | Val | Asp | Ile | Phe | Val | |
| | • | _ | | 330 | | | | | 335 | | | | • | 340 | | | |
| | | | | | | | | | | | | | | | | | |

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| | AGT | ACT | GTT | GAC | CCC | TTG | AAG | GAG | CCA | CCC | CTT | GTG | ACA | GCC | AAC | ACA | 1290 |
|----|-------|-------|-------|------|--------------|-----|-----------|------|------|------|-------|---|-----|-----|--------|------|------|
| | Ser | Thr | Val | Asp | Pro | Leu | Lys | Glu | Pro | Pro | Leu | Val | Thr | Ala | Asn | Thr | |
| | | | 345 | | | | | 350 | | | | | 355 | | | | |
| _ | | | | | | | | | | | | | | | | | |
| 3 | GTG | | | | | | | | | | | | | | | | 1338 |
| | Val | | Ser | He | Leu | Ala | | Asp | Tyr | Pro | Val | - | Lys | Val | Ser | Cys | |
| | | 360 | | | | | 365 | | | | | 370 | | | | | |
| | TAT | GTT | TCT | GAT | GAT | GGT | GCT | GCT | ATG | TTA | TCA | TTT | GAA | TCA | CTT | GCA | 1386 |
| 10 | Tyr | Val | Ser | Asp | Asp | Gly | Ala | Ala | Met | Leu | Ser | Phe | Glu | Ser | Leu | Ala | |
| | 375 | | | | | 380 | | | | | 385 | | | | | 390 | |
| | | | | | | | | | | | | | | | | | |
| | GAA | ACA | TCA | GAG | TTT | GCT | CGT | AAA | TGG | GTA | CCA | TTT | TGC | AAG | AAA | TAT | 1434 |
| | | Thr | Ser | Glu | Phe | Ala | Arg | Lув | Trp | Val | Pro | Phe | Cys | Lys | Lys | Tyr | |
| 15 | | | | | 395 | | | | | 400 | | | | | 405 | | |
| | N.C.C | n m n | C N C | | COM | CCA | CON | CD D | TCC. | ma c | ener. | COT | 000 | | n Tr n | GNW. | 1482 |
| | | | | | CGT Arg | | | | | | | | | | | | 1482 |
| | 501 | | 014 | 410 | 77. 9 | ALG | 110 | 014 | 415 | •,,- | | ,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,, | ALU | 420 | | wpb | |
| 20 |) | | | | | | | | | | | | | | | | |
| | TAC | TTG | AAG | GAT | AAA | GTT | CAG | ACA | TCA | TTT | GTC | AAA | GAT | CGT | AGA | GCT | 1530 |
| | Tyr | Leu | Lys | Asp | Lys | Val | Gln | Thr | Ser | Phe | Val | Lys | Asp | Arg | Arg | Ala | |
| | | | 425 | | | | | 430 | | | | | 435 | | | | |
| | | | | | | | | | | | | | | | | | |
| 25 | ATG | AAG | AGG | GAA | TAT | GAG | GAA | TTT | AAA | ATC | CGA | ATC | AAT | GCA | CTT | GTT | 1578 |
| | Met | - | Arg | Glu | Tyr | Glu | | Phe | Lys | Ile | Arg | | Asn | Ala | Leu | Val | |
| | | 440 | | | | | 445 | | | | | 450 | | | | | |
| | TCC | AAA | GCC | CT'A | AAA | TGT | CCT | GAD | 445 | GGG | ጥርር | רידים | ΔTG | ראא | CAT | GGC | 1626 |
| 30 | Ser | | | | | | | | | | | | | | | | 2020 |
| | 455 | • | | | • | 460 | | | | • | 465 | | | | • | 470 | |
| | | | | | | | | | | | | | | | | | |
| | ACA | CCG | TGG | CCT | GGA | AAT | AAT | ACA | GGG | GAC | CAT | CCA | GGA | ATG | ATC | CAG | 1674 |
| | | Pro | Trp | Pro | Gly | Asn | Asn | Thr | Gly | Asp | His | Pro | Gly | Met | Ile | Gln | |
| 35 | | | | | 475 | | | | | 480 | | | | | 485 | | |
| | | | | | | | | | | | | | | | | | |
| | | | | | CAA | | | | | | | | | | | | 1722 |
| | V a l | Phe | 1.011 | GIV | Gin | Agn | GIV | GIV | Leu | ARD | Ala | Glu | Gly | Asn | Glu | Len | |
| | V41 | | | 490 | J 1 | | 41 | , | 495 | F | | | , | 500 | | 204 | |

- 140 -

| | CCG | CGT | TTG | GTA | TAT | GTT | тст | CGA | GAA | AAG | CGA | CCA | GGA | TTC | CAG | CAC | 1770 |
|-----------|--------------------|-----|-----|-----|-----|-----|------|------|-----|------|-----|-----|--------|------|------|------|------|
| | Pro | Arg | Leu | Val | Tyr | Val | Ser | Arg | Glu | Lys | Arg | Pro | Gly | Phe | Gln | His | |
| | | | 505 | | | | | 510 | | | | | 515 | | | | |
| | | | | | | | | | | | | | | | | | |
| 5 | CAC | AAA | AAG | GCT | GGT | GCT | ATG | AAT | GCA | CTG | GTG | AGA | GTT | TCA | GCA | GTT | 1818 |
| | His | Lys | Lys | Ala | Gly | Ala | Met | Asn | Ala | Leu | Val | Arg | Val | Ser | Ala | Val | |
| | | 520 | | | | | 525 | | | | | 530 | | | | | |
| | | | | | | | | | | | | | | | | | |
| | | | | | CCT | | | | | | | | | | | | 1866 |
| 10 | Leu | Thr | Asn | Gly | Pro | Phe | Ile | Leu | Asn | Leu | Asp | Сув | Asp | His | Tyr | Ile | |
| | 535 | | | | | 540 | | | | | 545 | | | | | 550 | |
| | | | | | | | | | | | | | | | | | |
| | | | | | GCC | | | | | | | | | | | | 1914 |
| | Asn | naA | Ser | Lys | Ala | Leu | Arg | Glu | Ala | | Cys | Phe | Leu | Met | Asp | Pro | |
| 15 | | | | | 555 | | | | | 560 | | | | | 565 | | |
| | | | | | | | | | | | | | | | | | |
| | | | | | CAA | | | | | | | | | | | | 1962 |
| | Asn | Leu | GIY | _ | Gln | vaı | Cys | Tyr | | GIN | Phe | Pro | GIN | _ | Phe | Asp | |
| 20 | | | | 570 | | | | | 575 | | | | | 580 | | | |
| <i></i> ∨ | GGT | ልጥሮ | СУТ | ממ | AAC | CAT | aca. | ጥልጥ | CCT | አልጥ | CGT | አልጥ | » « | GTG. | ጥጥር | ጥጥጥ | 2010 |
| | _ | | | | Asn | | | | | | | | | | | | 2010 |
| | 4. <i>y</i> | *** | 585 | 2,0 | A0 | nop | my | 590 | ALG | ADII | nrg | non | 595 | Vai | FIIC | FIIC | |
| | | | | | | | | 2,70 | | | | | 3,3 | | | | |
| 25 | GAT | ATT | AAC | TTG | AGA | GGT | TTA | GAT | GGG | ATT | CAA | GGA | ССТ | GTA | ТАТ | GTC | 2058 |
| | | | | | Arg | | | | | | | | | | | | |
| | • | 600 | | | | 2 | 605 | | 1 | | | 610 | | | -,- | | |
| | | | | | | | | | | | | | | | | | |
| | GGA | ACT | GGA | TGT | GTT | TTC | AAC | AGA | ACA | GCA | TTA | TAC | GGT | TAT | GAA | CCT | 2106 |
| 30 | Gly | Thr | Gly | Cys | Val | Phe | Asn | Arg | Thr | Ala | Leu | Tyr | Gly | Tyr | Glu | Pro | |
| | 615 | | | | | 620 | | | | | 625 | - | • | - | | 630 | |
| | | | | | | | | | | | | | | | | | |
| | CCA | ATA | AAA | GTA | AAA | CAC | AAG | AAG | CCA | AGT | CTT | TTA | TCT | AAG | CTC | TGT | 2154 |
| | Pro | Ile | Lys | Val | Lys | His | Lys | Lys | Pro | Ser | Leu | Leu | Ser | Lys | Leu | Сув | |
| 35 | | | | | 635 | | | | | 640 | | | | | 645 | | |
| | | | | | | | | | | | | | | | | | |
| | GGT | GGA | TCA | AGA | AAG | AAG | AAT | TCC | AAA | GCT | AAG | AAA | GAG | TCG | GAC | AAA | 2202 |
| | Gly | Gly | Ser | Arg | Lys | Lys | Asn | Ser | Lys | Ala | Lys | Lys | Glu | Ser | Asp | Lys | |
| | | | | 650 | | | | | 655 | | | | | 660 | | | |
| 40 | | | | | | | | | | | | | | | | | |

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| | AAG | AAA | TCA | GGC | AGG | CAT | ACT | GAC | TCA | ACT | GTT | CCT | GTA | TTC | AAC | CTC | 2250 |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
| | Lys | Lys | Ser | Gly | Arg | His | Thr | Asp | Ser | Thr | Val | Pro | Val | Phe | Asn | Leu | |
| | | | 665 | | | | | 670 | | | | | 675 | | | | |
| | | | | | | | | | | | | | | | | | |
| 5 | GAT | GAC | ATA | GAA | GAG | GGA | GTT | GAA | GGT | GCT | GGT | TTT | GAT | GAT | GAA | AAG | 2298 |
| | Asp | Asp | Ile | Glu | Glu | Gly | Val | Glu | Gly | Ala | Gly | Phe | Asp | Asp | Glu | Lys | |
| | | 680 | | | | | 685 | | | | | 690 | | | | | |
| | | | | | | | | | | | | | | | | | |
| | GCG | CTC | TTA | ATG | TCG | CAA | ATG | AGC | CTG | GAG | AAG | CGA | TTT | GGA | CAG | TCT | 2346 |
| 10 | Ala | Leu | Leu | Met | Ser | Gln | Met | Ser | Leu | Glu | Lys | Arg | Phe | Gly | Gln | Ser | |
| | 695 | | | | | 700 | | | | | 705 | | | | | 710 | |
| | | | | | | | | | | | | | | | | | |
| | GCT | GTT | TTT | GTT | GCT | TCT | ACC | CTA | ATG | GAA | AAT | GGT | GGT | GTT | CCT | CCT | 2394 |
| | Ala | Val | Phe | Val | Ala | Ser | Thr | Leu | Met | Glu | Asn | Gly | Gly | Val | Pro | Pro | |
| 15 | | | | | 715 | | | | | 720 | | | | | 725 | | |
| | | | | | | | | | | | | | | | | | |
| | TCA | GCA | ACT | CCA | GAA | AAC | TTT | CTC | AAA | GAG | GCT | ATC | CAT | GTC | ATT | AGT | 2442 |
| | Ser | Ala | Thr | Pro | Glu | Asn | Phe | Leu | Lys | Glu | Ala | Ile | His | Val | Ile | Ser | |
| | | | | 730 | | | | | 735 | | | | | 740 | | | |
| 20 | | | | | | | | | | | | | | | | | |
| | TGT | GGT | TAT | GAG | GAT | AAG | TCA | GAT | TGG | GGA | ATG | GAG | ATT | GGA | TGG | ATC | 2490 |
| | Сув | Gly | Tyr | Glu | Asp | Lys | Ser | Asp | Trp | Gly | Met | Glu | lle | Gly | Trp | Ile | |
| | | | 745 | | | | | 750 | | | | | 755 | | | | |
| | | | | | | | | | | | | | | | | | |
| 25 | TAT | GGT | TCT | GTG | ACA | GAA | GAT | ATT | CTG | ACT | GGG | TTC | AAA | ATG | CAT | GCC | 2538 |
| | Tyr | Gly | Ser | Val | Thr | Glu | Asp | Ile | Leu | Thr | Gly | Phe | Lys | Met | His | Ala | |
| | | 760 | | | | | 765 | | | | | 770 | | | | | |
| | | | | | | | | | | | | | | | | | |
| | CGT | GGA | TGG | CGA | TCC | ATT | TAC | TGC | ATG | CCT | AAG | CTT | CCA | GCT | TTC | AAG | 2586 |
| 30 | Arg | Gly | Trp | Arg | Ser | Ile | Tyr | Сув | Met | Pro | Lys | Leu | Pro | Ala | Phe | Lys | |
| | 775 | | | | | 780 | | | | | 785 | | | | | 790 | |
| | | | | | | | | | | | | | | | | | |
| | GGT | TCT | GCT | CCT | ATC | AAT | CTT | TCA | GAT | CGT | CTG | AAC | CAA | GTG | CTG | AGG | 2634 |
| | Gly | Ser | Ala | Pro | Ile | Asn | Leu | Ser | Asp | Arg | Leu | Asn | Gln | Val | Leu | Arg | |
| 35 | | | | | 795 | | | | | 800 | | | | | 805 | | |
| | | | | | | | | | | | | | | | | | |
| | TGG | GCT | TTA | GGT | TCA | GTT | GAG | ATT | CTC | TTC | AGT | CGG | CAT | TGT | CCT | ATA | 2682 |
| | Trp | Ala | Leu | Gly | Ser | Val | Glu | Ile | Leu | Phe | Ser | Arg | His | Сув | Pro | Ile | |
| | | | | 810 | | | | | 815 | | | | | 820 | | | |

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| | TGG | TAT | GGT | TAC | AAT | GGG | AGG | CTA | AAA | TTT | CTT | GAG | AGG | TTT | GCG | TAT | 2730 |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|-----|------|
| | Trp | Tyr | Gly | Tyr | Asn | Gly | Arg | Leu | Lys | Phe | Leu | Glu | Arg | Phe | Ala | Tyr | |
| | | | 825 | | | | | 830 | | | | | 835 | | | | |
| | | | | | | | | | | | | | | | | | |
| 5 | GTG | AAC | ACC | ACC | ATC | TAC | CCT | ATC | ACC | TCC | ATT | CCT | CTT | CTC | ATG | TAT | 2778 |
| | Val | Asn | Thr | Thr | Ile | Tyr | Pro | Ile | Thr | Ser | Ile | Pro | Leu | Leu | Met | Tyr | |
| | | 840 | | | | | 845 | | | | | 850 | | | | | |
| | | | | | | | | | | | | | | | | | |
| 10 | | | | | | | | | | | | | TTT | | | | 2826 |
| 10 | Cys | Thr | Leu | Leu | AIA | | Cys | Leu | Pne | Inr | | GIN | Pne | TIE | 116 | | |
| | 855 | | | | | 860 | | | | | 865 | | | | | 870 | |
| | CAG | ТТА | AGT | AAC | ATT | GCA | AGT | ATA | TGG | ттт | CTG | тст | CTC | TTT | CTC | TCC | 2874 |
| | | | | | | | | | | | | | Leu | | | | |
| 15 | | | | | 875 | | | | • | 880 | | | | | 885 | | |
| | | | | | | | | | | | | | | | | | |
| | ATT | TTC | GCC | ACG | GGT | ATA | CTA | GAA | ATG | AGG | TGG | AGT | GGC | GTA | GGC | ATA | 2922 |
| | Ile | Phe | Ala | Thr | Gly | Ile | Leu | Glu | Met | Arg | Trp | Ser | Gly | Val | Gly | Ile | |
| | | | | 890 | | | | | 895 | | | | | 900 | | | |
| 20 | | | | | | | | | | | | | | | | | |
| | GAC | GAA | TGG | TGG | AGA | AAC | GAG | CAG | TTT | TGG | GTC | ATT | GGT | GGA | GTA | TCC | 2970 |
| | Asp | Glu | Trp | Trp | Arg | Asn | Glu | Gln | Phe | Trp | Val | Ile | Gly | Gly | Val | Ser | |
| | | | 905 | | | | | 910 | | | | | 915 | | | | |
| | | | | | | | | | | | | | | | | | |
| 25 | GCT | CAT | TTA | TTC | GCT | GTG | TTT | CAA | GGT | ATC | CTC | AAA | GTC | CTT | GCC | GGT | 3018 |
| | Ala | His | Leu | Phe | Ala | Val | Phe | Gln | Gly | Ile | Leu | Lys | Val | Leu | Ala | Gly | |
| | | 920 | | | | | 925 | | | | | 930 | | | | | |
| | | | | | | | | | | | | | | | | | |
| 20 | | | | | | | | | | | | | | | | GGA | 3066 |
| 30 | | Asp | Thr | Asn | Pne | | | Thr | Ser | Lys | | | Asp | GIU | Asp | Gly | |
| | 935 | | | | | 940 | | | | | 945 | | | | | 950 | |
| | GAC | ኬጥ | GCT | GAG | CTC | ТАС | ттс | ттс | ААА | таа | ACA | ACA | רדי | CTG | TTA: | CCG | 3114 |
| | | | | | | | | | | | | | | | | Pro | |
| 35 | • | | | | 955 | - | | | -,- | 960 | | | | | 965 | | |
| | | | | | | | | | | | | | | | | | |
| | CCA | ACG | ACG | CTG | CTC | ATT | GTA | AAC | TTA | GTG | GGA | GTI | GTT | GCA | GGA | GTC | 3162 |
| | Pro | Thr | Thr | Leu | Leu | Ile | Val | Asn | Leu | Val | Gly | Val | Val | Ala | Gly | Val | |
| | | | | 970 | | | | | 975 | | | | | 980 |) | | |
| | | | | | | | | | | | | | | | | | |

. 40

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| | TCT | TAT | GCT | ATC | AAC | AGT | GGA | TAC | CAA | TCA | TGG | GGA | CCA | CTC | TTT | GGT | 3210 |
|----|------|-----|-------|-------|-------|-------|----------------|----------|-------|--------|--------|-------|------------|------|-------|--------|------|
| | Ser | Tyr | Ala | Ile | Asn | Ser | Gly | Tyr | Gln | Ser | Trp | Gly | Pro | Leu | Phe | Gly | |
| | | | 985 | | | | | 990 | | | | | 995 | | | | |
| | | | | | | | | | | | | | | | | | |
| 5 | AAG | TTG | TTC | TTT | GCC | TTC | TGG | GTG | ATT | GTT | CAC | TTG | TAC | CCT | TTC | CTC | 3258 |
| | Lys | Leu | Phe | Phe | Ala | Phe | Trp | Val | Ile | Val | His | Leu | Tyr | Pro | Phe | Leu | |
| | | 100 | 0 | | | | 1009 | 5 | | | | 1010 |) | | | | |
| | | | | | | | | | | | | | | | | | |
| | | | | | | | | | CGG | | | | | | | | 3306 |
| 10 | | | Leu | Met | Gly | Arg | Gln | Asn | Arg | Thr | Pro | Thr | Ile | Val | Val | Val | |
| | 1015 | 5 | | | | 1020 |) | | | | 1029 | 5 | | | | 1030 | |
| | | | | | | | | | | | | | | | | | |
| | | | | | | | | | TTC | | | | | | | | 3354 |
| 15 | Trp | Ser | Val | Leu | | | Ser | Ile | Phe | | | Leu | Trp | Val | | | |
| 15 | | | | | 1039 | 5 | | | | 1040 | 0 | | | | 1049 | 5 | |
| | ~~~ | | • | | | | | | | | | | | | | | |
| | | | | | | | | | GGC | | | | | | | | 3402 |
| | Asp | PIO | Pne | 1050 | | Arg | vai | Thr | Gly | | Asp | me | Leu | | • | GIY | |
| 20 | | | | 105 | J | | | | 1059 | • | | | | 1060 |) | | |
| 20 | ΔΤΟ | ממ | ጥርጥ | ጥርኔል | אסממב | מבטר | יממי: יממי: | ייר מידי | T AC | وياسات | יייייי | 3 NGC | י ייייי בי | תתת | | | 3451 |
| | | Asn | | IOA | JANG | .on (| , Cruru | 1171 | 11 N | .crg | |) AGC | | vvv | | | 2421 |
| | | | 1065 | 5 | | | | | | | | | | | | | |
| | | | | - | | | | | | | | | | | | | |
| 25 | AAAA | CAC | AGA A | ATTT | AAAT? | ra Ti | TTTT | CATTO | G TT | TAT | TGT | TCAC | TTT | TT 1 | ACTT | TGTTG | 3511 |
| | | | | | | | | | | | | | | | | | |
| | TGTO | TAT | CTG 7 | rctg: | rtcgi | T CI | rrcro | TCT: | r GG1 | GTC | AATA | ATT1 | ATGI | GT A | AGAA? | TATATC | 3571 |
| | | | | | | | | | | | | | | | | | |
| | TTAC | TCT | AGT 1 | ract: | TTGG | AA AC | TTA | TAAT | KAA 1 | AGTG! | AAAG | CCA | | | | | 3614 |
| 30 | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | |
| | (2) | INF | ORMA | rion | FOR | SEQ | ID N | 10:10 |): | | | | | | | | |
| 35 | | | | | | | | | | | | | | | | | |
| | | 1 | (i) S | EQUE | ENCE | CHAF | CACTE | ERIST | rics: | | | | | | | | |
| | | | | (A) | LEN | GTH : | 106 | 55 an | nino | acid | is | | | | | | |

(B) TYPE: amino acid(D) TOPOLOGY: linear

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| | | () | .11 1 | OLEC | CULE | TYPE | E: pr | otei | ın | | | | | | | |
|----|------------|-----------|------------|------------|-----------|------------|------------|------------|------------|-----------|------------|--------------|------------|-----|-----------|------------|
| | | (> | (i) S | EQUE | ENCE | DESC | CRIPT | CION | SEC |] ID | NO:1 | L O : | | | | |
| 5 | Met 1 | Glu | Ser | Glu | Gly 5 | Glu | Thr | Ala | Gly | Lys 10 | Pro | Met | Lys | Asn | Ile 15 | Val |
| | Pro | Gln | Thr | Сув 20 | Gln | Ile | Cys | Ser | Asp 25 | Asn | Val | Gly | Lys | Thr | Val | Asp |
| 10 | Gly | Asp | _ | | Val | Ala | Сув | • | | Сув | Ser | Phe | | | Суз | Arg |
| 16 | Pro | - | 35 Tyr | Glu | Tyr | Glu | Arg | 40 Lys | Asp | Gly | Asn | | 45 Ser | Сув | Pro | Gln |
| 15 | Сув | 50 Lvs | Thr | Arq | Tvr | Lvs | 55 Arg | Leu | Lvs | Glv | Ser | 60 Pro | Ala | Ile | Pro | Glv |
| | - 65 | • | | J | • | 70 | _ | | • | • | 75 | | | | | 80 |
| 20 | Asp | Lys | Asp | Glu | Asp 85 | Gly | Leu | Ala | Asp | Glu 90 | Gly | Thr | Val | Glu | Phe 95 | Asn |
| | Tyr | Pro | Gln | Lys 100 | Glu | Lys | Ile | Ser | Glu 105 | Arg | Met | Leu | Gly | Trp | His | Leu |
| 25 | Thr | Arg | Gly 115 | Lys | Gly | Glu | Glu | Met 120 | Gly | Glu | Pro | Gln | Tyr 125 | Авр | Lys | Glu |
| 30 | Val | Ser | His | Asn | His | Leu | Pro 135 | Arg | Leu | Thr | Ser | Arg | Gln | Asp | Thr | Ser |
| | Gly 145 | Glu | Phe | Ser | Ala | Ala 150 | Ser | Pro | Glu | Arg | Leu 155 | | Val | Ser | Ser | Thr 160 |
| 35 | Ile | Ala | Gly | Gly | Lys | Arg | Leu | Pro | Tyr | Ser | | Asp | Val | Asn | Gln | |

Pro Asn Arg Arg Ile Val Asp Pro Val Gly Leu Gly Asn Val Ala Trp
180 185 190

165

40

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| | Lys | Glu | Arg | Val | Asp | Gly | Trp | Lys 200 | Met | Lys | Gln | Glu | Lys 205 | Asn | Thr | Gly |
|----|-----|-----|-----|--------------|-------------|--------------|-----|------------|------------|-------------|-----|------|------------|------------|-----|------|
| | | | | m. | 61 - | N 1 - | Ala | ° | C1 | > | C1 | Clu. | V-1 | Nan | 710 | N an |
| 5 | Pro | | ser | rnr | GIN | Ala | | ser | GIU | Arg | GIY | 220 | Val | Asp | 116 | wah |
| 5 | | 210 | | | | | 215 | | | | | 220 | | | | |
| | Ala | Ser | Thr | Asp | Ile | Leu | Ala | Asp | Glu | Ala | Leu | Leu | Asn | Asp | Glu | Ala |
| | 225 | | | | | 230 | | | | | 235 | | | | | 240 |
| 10 | Arq | Gln | Leu | Leu | Ser | Arg | Lys | Val | Ser | Ile | Pro | Ser | Ser | Arg | Ile | Asn |
| | | | | | 245 | | | | | 250 | | | | | 255 | |
| | | _ | | | | | | _ | _ | | | -1- | • | a | • | nh - |
| | Pro | Tyr | Arg | Met 260 | Val | 11e | Met | Leu | Arg 265 | Leu | vaı | 116 | Leu | Cys 270 | Leu | Pne |
| 15 | | | | 260 | | | | | 203 | | | | | 210 | | |
| | Leu | His | Tyr | Arg | Ile | Thr | naA | Pro | Val | Pro | Asn | Ala | Phe | Ala | Leu | Trp |
| | | | 275 | | | | | 280 | | | | | 285 | | | |
| | Lou | Val | Sar | Val | Tle | Cve | Glu | Tle | Trn | Dhe | Δla | Leu | Ser | Tro | Tle | Leu |
| 20 | Deu | 290 | 361 | val | 110 | Cys | 295 | 110 | 110 | 1110 | ALG | 300 | 001 | | | |
| | | | | | | | | | | | | | | | | |
| | Asp | Gln | Phe | Pro | Lys | Trp | Phe | Pro | Val | Asn | Arg | Glu | Thr | Tyr | Leu | Asp |
| | 305 | | | | | 310 | | | | | 315 | | | | | 320 |
| 25 | Ara | Leu | Ala | Leu | Ara | Tvr | Asp | Arg | Glu | Glv | Glu | Pro | Ser | Gln | Leu | Ala |
| | 5 | | | | 325 | -,- | | 3 | | 330 | | | | | 335 | |
| | | | | | | | | | | | | | | | | |
| | Ala | Val | Asp | | Phe | Val | Ser | Thr | | Asp | Pro | Leu | Lys | | Pro | Pro |
| 30 | | | | 340 | | | | | 345 | | | | | 350 | | |
| - | Leu | Val | Thr | Ala | Asn | Thr | Val | Leu | Ser | Ile | Leu | Ala | Val | Asp | Tyr | Pro |
| | | | 355 | | | | | 360 | | | | | 365 | | | |
| | | | _ | - | _ | _ | _ | | _ | _ | | | | | | _ |
| 25 | Val | - | Lys | Val | Ser | Сув | Tyr | Val | Ser | qaA | Asp | - | Ala | Ala | Met | Leu |
| 35 | | 370 | | | | | 375 | | | | | 380 | | | | |
| | Ser | Phe | Glu | Ser | Leu | Ala | Glu | Thr | Ser | Glu | Phe | Ala | Arg | Lys | Trp | Val |
| | 385 | | | | | 390 | | | | | 395 | | | | | 400 |

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| | Pro | Phe | Cys | Lys | Lys 405 | Tyr | Ser | Ile | Glu | Pro 410 | Arg | Ala | Pro | Glu | Trp 415 | Tyr |
|----|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|-------------|------------|------------|
| 5 | Phe | Ala | Ala | Lys 420 | Ile | Asp | Tyr | Leu | Lys 425 | Asp | Lys | Val | Gln | Thr 430 | Ser | Phe |
| | Val | Lys | Asp 435 | Arg | Arg | Ala | Met | Lys 440 | Arg | Glu | Tyr | Glu | Glu 445 | Phe | Lys | Ile |
| 10 | Arg | Ile 450 | Asn | Ala | Leu | Val | Ser 455 | Lys | Ala | Leu | Lув | Cys 460 | Pro | Gl u | Glu | Gly |
| 15 | Trp 465 | Val | Met | Gln | Asp | Gly 470 | Thr | Pro | Trp | Pro | Gly 475 | Asn | Asn | Thr | Gly | Asp 480 |
| | Н16 | Pro | Gly | Met | Ile 485 | Gln | Val | Phe | Leu | Gly 490 | Gln | Asn | Gly | Gly | Leu 495 | Asp |
| 20 | Ala | Glu | Gly | Asn 500 | Glu | Leu | Pro | Arg | Leu 505 | Val | Tyr | Val | Ser | Arg 510 | Glu | Lys |
| | Arg | Pro | Gly 515 | Phe | Gln | His | His | Lys 520 | Lys | Ala | Gly | Ala | Met 525 | Asn | Ala | Leu |
| 25 | Val | Arg 530 | Val | Ser | Ala | Val | Leu 535 | Thr | Asn | Gly | Pro | Phe 540 | Ile | Leu | Asn | Leu |
| 30 | Asp 545 | Суз | Asp | His | Tyr | Ile 550 | Asn | Asn | Ser | Lys | Ala 555 | Leu | Arg | Glu | Ala | Met 560 |
| | | | | | 565 | Pro | | | | 570 | | | | | 575 | |
| 35 | | | | 580 | | Asp | · | | 585 | - | | - | | 590 | | |
| | Arg | Asn | Thr 595 | | Phe | Phe | Asp | Ile | | Leu | Arg | Gly | Leu 605 | | Gly | Ile |

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| | Gln | Gly | Pro | Val | Tyr | Val | Gly | Thr | Gly | Cys | Val | Phe | Asn | Arg | Thr | Ala |
|----|--------|----------|-----|------|------|-----|-----|-----|----------|-----|-----|-------------|-----|-----|------|--------------|
| | | 610 | | | | | 615 | | | | | 620 | | | | |
| | | | | | | | | | | | | | | | | |
| | Leu | Tyr | Gly | Tyr | Glu | Pro | Pro | Ile | Lys | Val | Lys | His | Lys | Lys | Pro | Ser |
| 5 | 625 | | | | | 630 | | | | | 635 | | | | | 640 |
| | | | | | | | | | | | | | | | | |
| | Leu | Leu | Ser | Lvs | Leu | Cys | Gly | Gly | Ser | Arg | Lys | Lys | Asn | Ser | Lys | Ala |
| | | | | -,- | 645 | • | • | - | | 650 | - | - | | | 655 | |
| | | | | | | | | | | | | | | | | |
| 10 | Lare | Taya | Glu | Ser | Asn | Lvs | Lvs | Lvs | Ser | Glv | Arq | His | Thr | Asp | Ser | Thr |
| 10 | - Dy O | _ | 010 | 660 | 110p | 2,0 | -1- | -,- | 665 | 2 | | | | 670 | | |
| | | | | 000 | | | | | | | | | | | | |
| | 17-1 | Dro | บรา | Dho | Agn | Len | Aen | Δen | Tle | Glu | Glu | Glv | Val | Glu | Glv | Ala |
| | Val | FIO | 675 | FIIC | ASII | DCu | Aop | 680 | ••• | 010 | | , | 685 | | , | |
| 15 | | | 6/5 | | | | | 000 | | | | | 003 | | | |
| 13 | | | _ | | | | | • | 7 | | 0 | ~1 ~ | Mat | Co= | T ou | Clu |
| | Gly | | Asp | Asp | GIu | rys | | Leu | Leu | met | ser | | Mec | Ser | ьеu | GIU |
| | | 690 | | | | | 695 | | | | | 700 | | | | |
| | | | | | | _ | | | | | | | mh | • | W | 61. . |
| 20 | _ | Arg | Phe | Gly | Gin | | Ala | vai | Pne | vaı | | ser | inr | Leu | met | |
| 20 | 705 | | | | | 710 | | | | | 715 | | | | | 720 |
| | | | | | | | | | | | | | | _ | _ | |
| | Asn | Gly | Gly | Val | Pro | Pro | Ser | Ala | Thr | | | Asn | Phe | Leu | | GIU |
| | | | | | 725 | | | | | 730 | | | | | 735 | |
| | | | | | | | | | | | | | | | | |
| 25 | Ala | Ile | His | Val | Ile | Ser | Сув | Gly | Tyr | Glu | qaA | Lys | Ser | Asp | Trp | Gly |
| | | | | 740 | | | | | 745 | | | | | 750 | | |
| | | | | | | | | | | | | | | | | |
| | Met | Glu | Ile | Gly | Trp | Ile | Tyr | Gly | Ser | Val | Thr | Glu | Asp | Ile | Leu | Thr |
| | | | 755 | | | | | 760 | | | | | 765 | | | |
| 30 | | | | | | | | | | | | | | | | |
| | Gly | Phe | Lys | Met | His | Ala | Arg | Gly | Trp | Arg | Ser | Ile | Tyr | Сув | Met | Pro |
| | | 770 | | | | | 775 | | | | | 780 | | | | |
| | | | | | | | | | | | | | | | | |
| | Lys | Leu | Pro | Ala | Phe | Lys | Gly | Ser | Ala | Pro | Ile | Asn | Leu | Ser | Авр | Arg |
| 35 | 785 | | | | | 790 | | | | | 795 | | | | | 800 |
| | | | | | | | | | | | | | | | | |
| | Leu | Asn | Gln | Val | Leu | Ara | Tro | Ala | Leu | Gly | Ser | Val | Glu | Ile | Leu | Phe |
| | | | | _ | 805 | | - 4 | | | 810 | | | | | 815 | |
| | | | | | | | | | | | | | | | | |

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| | Ser | Arg | His | Суз | Pro | Ile | Trp | Tyr | Gly | Tyr | Asn | Gly | Arg | Leu | Lys | Phe |
|-----|-------------|-----|-----|-----|------------|-------------|------|------|------|-----|-----------|-------------|------|------|----------|------|
| | | | | 820 | | | | | 825 | | | | | 830 | | |
| | | | | | | | | | | | | | | | | |
| | Leu | Glu | Arg | Phe | Ala | Tyr | Val | Asn | Thr | Thr | Ile | Tyr | Pro | Ile | Thr | Ser |
| 5 | | | 835 | | | | | 840 | | | | | 845 | | | |
| | | | | | | | | | | | | | | | | |
| | Ile | Pro | Leu | Leu | Met | Tyr | Сув | Thr | Leu | Leu | Ala | Val | Cys | Leu | Phe | Thr |
| | | 850 | | | | | 855 | | | | | 860 | | | | |
| | | | | | | | | | | | | | | | | |
| 10 | Asn | Gln | Phe | Ile | Ile | Pro | Gln | Ile | Ser | Asn | Ile | Ala | Ser | Ile | Trp | Phe |
| | 865 | | | | | 870 | | | | | 875 | | | | _ | 880 |
| | | | | | | | | | | | | | | | | |
| | Leu | Ser | Leu | Phe | Leu | Ser | Ile | Phe | Ala | Thr | Glv | Ile | Leu | Glu | Met | Arq |
| | | | | | 885 | | | | | 890 | | | | | 895 | , |
| 15 | | | | | | | | | | | | | | | | |
| ••• | Tro | Ser | Glv | Val | Glv | Ile | Asp | Glu | Trp | Trp | Ara | Ann | Glu | Gln | Phe | Tro |
| | | | , | 900 | , | | 1102 | | 905 | | 3 | ••••• | | 910 | ••• | |
| | | | | | | | | | | | | | | | | |
| | Val | Ile | Glv | Glv | Val | Ser | Ala | His | Leu | Phe | Ala | Val | Phe | Gln | Glv | Ile |
| 20 | | | 915 | | | | | 920 | | | | | 925 | | 1 | |
| | | | | | | | | | | | | | | | | |
| | Leu | Lys | Val | Len | Ala | Glv | Ile | Asp | Thr | Asn | Phe | Thr | Va1 | Thr | Ser | ī.vs |
| | | 930 | *** | | | U 1, | 935 | лор | | | • • • • • | 940 | | •••• | 001 | 2,0 |
| | | 930 | | | | | 933 | | | | | 240 | | | | |
| 25 | 81 a | Ser | Ann | G1 | Nan | G) v | y an | Dho | NI a | Gl. | Lou | Τ | Lou | Dho | Lvo | Trn |
| 23 | | Ser | Asp | Gru | veb | 950 | Asp | FILE | YIG | GIU | 955 | lyt | Deu | FIIC | цув | |
| | 945 | | | | | 950 | | | | | 300 | | | | | 960 |
| | m\ | m) | • | • | . . | D | D | mh | mъ | • | | 7 1. | 17-1 | 3 | • | v-1 |
| | Inr | Thr | Leu | Leu | | Pro | Pro | inr | inr | | Leu | 116 | vaı | ABN | | vaı |
| 20 | | | | | 965 | | | | | 970 | | | | | 975 | |
| 30 | | | | | | | _ | _ | | | _ | _ | | _ | - | _ |
| | Gly | Val | Val | | Gly | Val | Ser | Tyr | | Ile | Asn | Ser | Gly | | Gln | Ser |
| | | | | 980 | | | | | 985 | | | | | 990 | | |
| | | | | | | | | | | | | | | | | |
| | Trp | Gly | Pro | Leu | Phe | Gly | Lys | Leu | Phe | Phe | Ala | Phe | Trp | Val | Ile | Val |
| 35 | | | 995 | | | | | 100 | 0 | | | | 100 | 5 | | |
| | | | | | | | | | | | | | | | | |
| | His | Leu | Tyr | Pro | Phe | Leu | Lys | Gly | Leu | Met | Gly | Arg | Gln | Asn | Arg | Thr |
| | | 101 | 0 | | | | 101 | 5 | | | | 102 | 0 | | | |

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Pro Thr Ile Val Val Val Trp Ser Val Leu Leu Ala Ser Ile Phe Ser 1030 1035 1040 1025 Leu Leu Trp Val Arg Ile Asp Pro Phe Thr Ser Arg Val Thr Gly Pro 5 1050 1045 Asp Ile Leu Glu Cys Gly Ile Asn Cys 1065 1060 10 (2) INFORMATION FOR SEQ ID NO:11: (i) SEQUENCE CHARACTERISTICS: 15 (A) LENGTH: 3673 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear 20 (ii) MOLECULE TYPE: cDNA (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 25 (vi) ORIGINAL SOURCE:

(A) ORGANISM: Arabidopsis thaliana

(B) STRAIN: Columbia

(C) INDIVIDUAL ISOLATE: rswl mutant

30

(ix) FEATURE:

(A) NAME/KEY: CDS

(B) LOCATION: 71..3313

35

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:11:

GAATCGGCTA CGAATTTCCC AATTTTGAAT TTTGTGAATC TCTCTCTTTC TCTGTGTGTC

- 150 -

| | GGTG | GCTC | GCG A | ATG (| GAG (| GCC A | AGT (| SCC (| GC : | TTG (| STT (| GCT (| GA 1 | rcc : | rac (| CGG | 109 |
|----|------|------|-------|-------|-------|-------|-------|-------|-------|-------|--------------|-------|-------|-------|-------|--------------|-----|
| | | | 0 | det (| Glu 1 | Ala S | Ser A | Ala (| Gly I | Leu \ | /al / | Ala (| Sly S | Ser : | Cyr 1 | Arg | |
| | | | | 1 | | | | 5 | | | | | 10 | | | | |
| 5 | | | | | | | | | | | | | | | | | |
|) | | | | | GTT | | | | | | | | | | | | 157 |
| | Arg | 15 | GIU | rea | Val | Arg | 20 | Arg | пів | GIU | ser | 25 | GIY | GIY | Inr | гÀè | |
| | | 23 | | | | | | | | | | | | | | | |
| | CCT | TTG | AAG | AAT | ATG | AAT | GGC | CAG | ATA | TGT | CAG | ATC | TGT | GGT | GAT | GAT | 205 |
| 10 | Pro | Leu | Lys | Asn | Met | Asn | Gly | Gln | Ile | Суз | Gln | Ile | Cys | Gly | Asp | Asp | |
| | 30 | | | | | 35 | | | | | 40 | | | | | 45 | |
| | | | | | | | | | | | | | | | | | |
| | GTT | GGA | CTC | GCT | GAA | ACT | GGA | GAT | GTC | TTT | GTC | GCG | TGT | AAT | GAA | TGT | 253 |
| | Val | Gly | Leu | Ala | Glu | Thr | Gly | Asp | Val | Phe | Val | Ala | Cys | Asn | Glu | Сув | |
| 15 | | | | | 50 | | | | | 55 | | | | | 60 | | |
| | ccc | ጥጥር | CCT | CTC | TGT | ccc | ССТ | TCC | ייאיי | CNC | ጥ ል ር | CAC | NCC. | *** | CNT | CCA | 301 |
| | | | | | Сув | | | | | | | | | | | | 301 |
| | | | | 65 | - | | | -,, | 70 | 010 | .,. | 014 | n.y | 75 | лор | 0. .y | |
| 20 | | | | | | | | | | | | | | | | | |
| | ACT | CAG | TGT | TGC | CCT | CAA | TGC | AAG | ACT | AGA | TTC | AGA | CGA | CAC | AGG | GGG | 349 |
| | Thr | Gln | Cys | Cys | Pro | Gln | Cys | Lys | Thr | Arg | Phe | Arg | Arg | His | Arg | Gly | |
| | | | 80 | | | | | 85 | | | | | 90 | | | | |
| | | | | | | | | | | | | | | | | | |
| 25 | | | | | GAA | | | | | | | | | | | | 397 |
| | Ser | | Arg | Val | Glu | Gly | | Glu | Asp | Glu | Asp | _ | Val | Asp | Asp | Ile | |
| | | 95 | | | | | 100 | | | | | 105 | | | | | |
| | GAG | ААТ | GAG | TTC | AAT | TAC | GCC | CAG | GGA | GCT | AAC | AAG | GCG | AGA | CAC | CAA | 445 |
| 30 | | | | | Asn | | | | | | | | _ | | | | |
| | 110 | | | | | 115 | | | - | | 120 | • | | | | 125 | |
| | | | | | | | | | | | | | | | | | |
| | CGC | CAT | GGC | GAA | GAG | TTT | TCT | TCT | TCC | TCT | AGA | CAT | GAA | TCT | CAA | CCA | 493 |
| | Arg | His | Gly | Glu | Glu | Phe | Ser | Ser | Ser | Ser | Arg | His | Glu | Ser | Gln | Pro | |
| 35 | | | | | 130 | | | | | 135 | | | | | 140 | | |
| | | | | | | | | | | | | | | | | | |
| | | | | | ACC | | | | | | | | | | | | 541 |
| | ile | Pro | Leu | | Thr | His | Gly | His | | | Ser | Gly | Glu | | Arg | Thr | |
| 40 | | | | 145 | • | | | | 150 | | | | | 155 | | | |
| 40 | | | | | | | | | | | | | | | | | |

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| | CCT | GAT | ACA | CAA | TCT | GTG | CGA | ACT | ACA | TCA | GGT | CCT | TTG | GGT | CCT | TCT | 589 |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
| | Pro | Asp | Thr | Gln | Ser | Val | Arg | Thr | Thr | Ser | Gly | Pro | Leu | Gly | Pro | Ser | |
| | | | 160 | | | | | 165 | | | | | 170 | | | | |
| | | | | | | | | | | | | | | | | | |
| 5 | GAC | AGG | AAT | GCT | ATT | TCA | TCT | CCA | TAT | ATT | GAT | CCA | CGG | CAA | CCT | GTC | 637 |
| | Asp | Arg | Asn | Ala | Ile | Ser | Ser | Pro | Tyr | Ile | Asp | Pro | Arg | Gln | Pro | Val | |
| | | 175 | | | | | 180 | | | | | 185 | | | | | |
| | | | | | | | | | | | | | | | | | |
| | CCT | GTA | AGA | ATC | GTG | GAC | CCG | TCA | AAA | GAC | TTG | AAC | TCT | TAT | GGG | CTT | 685 |
| 10 | Pro | Val | Arg | Ile | Val | Asp | Pro | Ser | Lys | Asp | Leu | Asn | Ser | Tyr | Gly | Leu | |
| | 190 | | | | | 195 | | | | | 200 | | | | | 205 | |
| | | | | | | | | | | | | | | | | | |
| | GGT | AAT | GTT | GAC | TGG | AAA | GAA | AGA | GTT | GAA | GGC | TGG | AAG | CTG | AAG | CAG | 733 |
| | Gly | Asn | Val | Asp | Trp | Lys | Glu | Arg | Val | Glu | Gly | Trp | Lys | Leu | Lys | Gln | |
| 15 | | | | | 210 | | | | | 215 | | | | | 220 | | |
| | | | | | | | | | | | | | | | | | |
| | GAG | AAA | AAT | ATG | TTA | CAG | ATG | ACT | GGT | AAA | TAC | CAT | GAA | GGG | AAA | GGA | 781 |
| | Glu | Lys | Asn | Met | Leu | Gln | Met | Thr | Gly | Lys | Tyr | His | Glu | Gly | Lys | Gly | |
| | | | | 225 | | | | | 230 | | | | | 235 | | | |
| 20 | | | | | | | | | | | | | | | | | |
| | GGA | GAA | ATT | GAA | GGG | ACT | GGT | TCC | AAT | GGC | GAA | GAA | CTC | CAA | ATG | GCT | 829 |
| | Gly | Glu | Ile | Glu | Gly | Thr | Gly | Ser | Asn | Gly | Glu | Glu | Leu | Gln | Met | Ala | |
| | | | 240 | | | | | 245 | | | | | 250 | | | | |
| | | | | | | | | | | | | | | | | | |
| 25 | GAT | GAT | ACA | CGT | CTT | CCT | ATG | AGT | CGT | GTG | GTG | CCT | ATC | CCA | TCT | TCT | 877 |
| | Asp | Asp | Thr | Arg | Leu | Pro | Met | Ser | Arg | Val | Val | Pro | Ile | Pro | Ser | Ser | |
| | | 255 | | | | | 260 | | | | | 265 | | | | | |
| | | | | | | | | | | | | | | | | | |
| | CGC | CTA | ACC | CCT | TAT | CGG | GTT | GTG | ATT | ATT | CTC | CGG | CTT | ATC | ATC | TTG | 925 |
| 30 | Arg | Leu | Thr | Pro | Tyr | Arg | Val | Val | Ile | Ile | Leu | Arg | Leu | Ile | Ile | Leu | |
| | 270 | | | | | 275 | | | | | 280 | | | | | 285 | |
| | | | | | | | | | | | | | | | | | |
| | TGT | TTC | TTC | TTG | CAA | TAT | CGT | ACA | ACT | CAC | CCT | GTG | AAA | AAT | GCA | TAT | 973 |
| | Cys | Phe | Phe | Leu | Gln | Tyr | Arg | Thr | Thr | His | Pro | Val | Lys | Asn | Ala | Tyr | |
| 35 | | | | | 290 | | | | | 295 | | | | | 300 | | |
| | | | | | | | | | | | | | | | | | |
| | CCT | TTG | TGG | TTG | ACC | TCG | GTT | ATC | TGT | GAG | ATC | TGG | TTT | GCA | TTT | TCT | 1021 |
| | Pro | Leu | Trp | Leu | Thr | Ser | Val | Ile | Cys | Glu | Ile | Trp | Phe | Ala | Phe | Ser | |
| | | | | 305 | | | | | 310 | | | | | 315 | | | |
| | | | | | | | | | | | | | | | | | |

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| | TGG | CTT | CTT | GAT | CAG | TTT | CCC | AAA | TGG | TAC | CCC | TTA | AAC | AGG | GAG | ACT | 1069 |
|----|-----|-------|-----|-------|-------|-------|-----|-----|-----|-----|-------|-----|-----|------|-------|-----|------|
| | Trp | Leu | Leu | qaA | Gln | Phe | Pro | Lys | Trp | Tyr | Pro | Ile | Asn | Arg | Glu | Thr | |
| | | | 320 | | | | | 325 | | | | | 330 | | | | |
| | | | | | | | | | | | | | | | | | |
| 5 | TAT | CTT | GAC | CGT | CTC | GCT | ATA | AGA | TAT | GAT | CGA | GAC | GGT | GAA | CCA | TCA | 1117 |
| | Tyr | Leu | Asp | Arg | Leu | Ala | Ile | Arg | Tyr | Asp | Arg | Asp | Gly | Glu | Pro | Ser | |
| | | 335 | | | | | 340 | | | | | 345 | | | | | |
| | | | | | | | | | | | | | | | | | |
| | CAG | CTC | GTT | CCT | GTT | GAT | GTG | TTT | GTT | AGT | ACA | GTG | GAC | CCA | TTG | AAA | 1165 |
| 10 | Gln | Leu | Val | Pro | Val | Asp | Val | Phe | Val | Ser | Thr | Val | Asp | Pro | Leu | Lys | |
| | 350 | | | | | 355 | | | | | 360 | | | | | 365 | |
| | | | | | | | | | | | | | | | | | |
| | GAG | ССТ | CCC | CTT | GTT | ACA | GCA | AAC | ACA | GTT | CTC | TCG | ATT | CTT | TCT | GTG | 1213 |
| | Glu | Pro | Pro | Leu | Val | Thr | Ala | Asn | Thr | Val | Leu | Ser | Ile | Leu | Ser | Val | |
| 15 | | | | | 370 | | | | | 375 | | | | | 380 | | |
| | | | | | | | | | | | | | | | | | |
| | GAC | TAC | CCG | GTA | GAT | AAA | GTA | GCC | TGT | TAT | GTT | TCA | GAT | GAT | GGT | TCA | 1261 |
| | Asp | Tyr | Pro | Val | Asp | ГЛа | Val | Ala | Cys | Tyr | Val | Ser | Asp | Asp | Gly | Ser | |
| | | | | 385 | | | | | 390 | | | | | 395 | | | |
| 20 | | | | | | | | | | | | | | | | | |
| | GCT | ATG | CTT | ACC | TTT | GAA | TCC | CTT | TCT | GAA | ACC | GCT | GAG | TTT | GCA | AAG | 1309 |
| | Ala | Met | Leu | Thr | Phe | Glu | Ser | Leu | Ser | Glu | Thr | Ala | Glu | Phe | Ala | Lys | |
| | | | 400 | | | | | 405 | | | | | 410 | | | | |
| | | | | | | | | | | | | | | | | | |
| 25 | AAA | TGG | GTA | CCA | TTT | TGC | AAG | AAA | TTC | AAC | ATT | GAA | ССТ | AGG | GCC | CCT | 1357 |
| | Lys | Trp | Val | Pro | Phe | Cys | Lys | Lys | Phe | Asn | Ile | Glu | Pro | Arg | Ala | Pro | |
| | | 415 | | | | | 420 | | | | | 425 | | | | | |
| | | | | | | | | | | | | | | | | | |
| | GAA | TTC | TAT | TTT | GCC | CAG | AAG | ATA | GAT | TAC | TTG | AAG | GAC | AAG | ATC | CAA | 1405 |
| 30 | Glu | Phe | Tyr | Phe | Ala | Gln | Lys | Ile | Asp | Tyr | Leu | Lys | Asp | Lys | Ile | Gln | |
| | 430 | | | | | 435 | | | | | 440 | | | | | 445 | |
| | | | | | | | | | | | | | | | | | |
| | CCG | TCI | TTT | GTI | · AAA | GAG | CGA | CGA | GCT | ATG | AAG | AGA | GAG | TAT | GAA | GAG | 1453 |
| | Pro | Ser | Phe | . Val | Lys | Glu | Arg | Arg | Ala | Met | Lys | Arg | Glu | Туг | Glu | Glu | |
| 35 | | | | | 450 |) | | | | 455 | | | | | 460 | ı | |
| | | | | | | | | | | | | | | | | | |
| | TTT | ' AAA | GTG | AGG | ATA | TAA A | GCI | CTI | GTT | GCC | : AAA | GC# | CAG | AA a | A ATC | CCT | 1501 |
| | Phe | . Lys | val | Arg | , Ile | . Asn | Ala | Leu | Val | Ala | Lys | Ala | Glr | Lys | ıle | Pro | |
| | | | | 465 | 5 | | | | 470 | I | | | | 475 | 5 | | |
| 40 |) | | | | | | | | | | | | | | | | |

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| | GAA | GAA | GGC | TGG | ACA | ATG | CAG | GAT | GGT | ACT | ccc | TGG | CCT | GGT | AAC | AAC | 1549 |
|-----|------|------|-----|------|-----|------------|------|-------------|-----|-----|--------------|-----|------|-----|---------|-------|------|
| | Glu | Glu | Gly | Trp | Thr | Met | Gln | Asp | Gly | Thr | Pro | Trp | Pro | Gly | Asn | Asn | |
| | | | 480 | | | | | 485 | | | | | 490 | | | | |
| | | | | | | | | | | | | | | | | | |
| 5 | ACT | AGA | GAT | CAT | ССТ | GGA | ATG | ATA | CAG | GTG | TTC | TTA | GGC | CAT | AGT | GGG | 1597 |
| _ | | | Asp | | | | | | | | | | | | | | |
| | •••- | 495 | | | | , | 500 | | | | | 505 | , | | | , | |
| | | •,,, | | | | | 500 | | | | | | | | | | |
| | CCT | CTG | GAT | ACC | GAT | GGA | таа | GAG | ста | ССТ | AGA | CTC | ATC | ТАТ | GTT | тст | 1645 |
| 10 | | - | Asp | | | | | | | | | | | | | | |
| 10 | - | Deu | voh | 1111 | vab | 515 | 7011 | 01 0 | DCu | | 520 | Deu | | | *** | 525 | |
| | 510 | | | | | 212 | | | | | 520 | | | | | 323 | |
| | ~~ | ~~~ | | 000 | 000 | 663 | mmm | CAA | CNC | CNC | | 220 | CCT | CCX | COT | N.T.C | 1693 |
| | | | AAG | | | | | | | | | | | | | | 1033 |
| 1.5 | Arg | GIU | ГÀв | Arg | | GIY | Pne | GIN | nıs | | rys | Lys | AIG | GIY | | MEL | |
| 15 | | | | | 530 | | | | | 535 | | | | | 540 | | |
| | | | | | | | | | | | | | | | | | |
| | | | TTG | | | | | | | | | | | | | | 1741 |
| | Asn | Ala | Leu | Ile | Arg | Val | Ser | Val | Val | Leu | Thr | Asn | Gly | Ala | Tyr | Leu | |
| | | | | 545 | | | | | 550 | | | | | 555 | | | |
| 20 | | | | | | | | | | | | | | | | | |
| | TTG | AAC | GTG | GAT | TGT | GAT | CAT | TAC | TTT | AAT | AAC | AGT | AAG | GCT | ATT | AAA | 1789 |
| | Leu | Asn | Val | Asp | Cys | Asp | His | Tyr | Phe | Asn | Asn | Ser | Lys | Ala | Ile | Lys | |
| | | | 560 | | | | | 565 | | | | | 570 | | | | |
| | | | | | | | | | | | | | | | | | |
| 25 | GAA | GCT | ATG | TGT | TTC | ATG | ATG | GAC | CCG | GCT | ATT | GGA | AAG | AAG | TGC | TGC | 1837 |
| | Glu | Ala | Met | Cys | Phe | Met | Met | Авр | Pro | Ala | Ile | Gly | Lys | Lys | Сув | Сув | |
| | | 575 | | | | | 580 | | | | | 585 | | | | | |
| | | | | | | | | | | | | | | | | | |
| | TAT | GTC | CAG | TTC | CCT | CAA | CGT | TTT | GAC | GGT | ATT | GAT | TTG | CAC | GAT | CGA | 1885 |
| 30 | Tyr | Val | Gln | Phe | Pro | Gln | Arg | Phe | Asp | Gly | Ile | Asp | Leu | His | Asp | Arg | |
| | 590 | | | | | 595 | | | | | 600 | | | | | 605 | |
| | | | | | | | | | | | | | | | | | |
| | TAT | GCC | AAC | AGG | AAT | ATA | GTC | TTT | TTC | GAT | ATT | AAC | ATG | AAG | GGG | TTG | 1933 |
| | | | Asn | | | | | | | | | | | | | | |
| 35 | -,- | | | | 610 | | | | | 615 | | | | -,- | 620 | | |
| | | | | | -20 | | | | | | | | | | | | |
| | מיים | CCT | ATC | CNC | COT | רכי | ርጥኦ | ጥአጥ | ርሞር | ርረጥ | <u>አ</u> ርሳጥ | COM | ምረነጥ | سنک | dodocto | ייממ | 1981 |
| | | | | | | | | | | | | | | | | | 1301 |
| | Asp | GIÀ | TIE | | GIĄ | PIO | vai | īĀī | | GIÀ | ınr | GIÀ | cys | - | rne | Aan | |
| 40 | | | | 625 | | | | | 630 | | | | | 635 | | | |
| 40 | | | | | | | | | | | | | | | | | |

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| | AGG | CAG | GCT | CTA | TAT | GGG | TAT | GAT | CCT | GTT | TTG | ACG | GAA | GAA | GAT | ATT | 2029 |
|-----|-----|-----------|-----|------------|-----------------|----------|--------------|-----|-----|------|---|---------|---------|-----|------|------|------|
| | Arg | Gln | Ala | Leu | Tyr | Gly | Tyr | Asp | Pro | Val | Leu | Thr | Glu | Glu | Asp | Leu | |
| | | | 640 | | | | | 645 | | | | | 650 | | | | |
| | | | | | | | | | | | | | | | | | |
| 5 | GAA | CCA | TAA | ATT | ATT | GTC | AAG | AGC | TGT | TGC | GGG | TCA | AGG | AAG | AAA | GGT | 2077 |
| | Glu | Pro | Asn | Ile | Ile | Val | Lys | Ser | Cys | Cys | Gly | Ser | Arg | ГЛя | Lys | Gly | |
| | | 655 | | | | | 660 | | | | | 665 | | | | | |
| | | | | | | | | | | | | | | | | | |
| • • | | | | AAG | | | | | | | | | | | | | 2125 |
| 10 | Lys | Ser | Ser | ГÀа | Lys | Tyr | Asn | Tyr | Glu | Lys | Arg | Arg | Gly | Ile | naA | Arg | |
| | 670 | | | | | 675 | | | | | 680 | | | | | 685 | |
| | | | | | | | | | | | | | | | | | |
| | | | | AAT | | | | | | | | | | | | | 2173 |
| 1.5 | Ser | Asp | Ser | Asn | | Pro | Leu | Phe | Asn | | Glu | Asp | Ile | Asp | | Gly | |
| 15 | | | | | 690 | | | | | 695 | | | | | 700 | | |
| | mm | ~~ | | | a | C. T. T. | a.a | 200 | | 3 mm | Om n | | | | | | |
| | | | | TAT | | | | | | | | | | | | | 2221 |
| | Pne | GIU | GIY | Tyr 705 | Asp | Asp | GIU | Arg | | 116 | Leu | met | ser | | Arg | Ser | |
| 20 | | | | 705 | | | | | 710 | | | | | 715 | | | |
| 20 | СТА | GAG | DAG | CGT | արդուր Մարես | CCT | CAG | TCG | CCG | СТА | արագրագրայուն անույլու անույ | አ ጥጥ | aca | GCN | ልሮሮ | TTC | 2269 |
| | | | | Arg | | | | | | | | | | | | | 2209 |
| | ••• | 010 | 720 | 9 | - 110 | Cly | U 111 | 725 | 710 | 141 | rne | 116 | 730 | via | 1111 | FILE | |
| | | | | | | | | | | | | | .50 | | | | |
| 25 | ATG | GAA | CAA | GGC | GGC | ATT | CCA | CCA | ACA | ACC | AAT | ccc | GCT | ACT | CTT | CTG | 2317 |
| | | | | Gly | | | | | | | | | | | | | |
| | | 735 | | • | • | | 740 | | | | | 745 | | | | | |
| | | | | | | | | | | | | | | | | | |
| | AAG | GAG | GCT | ATT | CAT | GTT | ATA | AGC | TGT | GGT | TAC | GAA | GAC | AAG | ACT | GAA | 2365 |
| 30 | Lys | Glu | Ala | Ile | His | Val | Ile | Ser | Сув | Gly | Tyr | Glu | Asp | Lys | Thr | Glu | |
| | 750 | | | | | 755 | | | | | 760 | | | | | 765 | |
| | | | | | | | | | | | | | | | | | |
| | TGG | GGC | AAA | GAG | ATT | GGT | TGG | ATC | TAT | GGT | TCC | GTG | ACG | GAA | GAT | TTA | 2413 |
| | Trp | Gly | Lys | Glu | Ile | Gly | Trp | Ile | Tyr | Gly | Ser | Val | Thr | Glu | Asp | Ile | |
| 35 | | | | | 770 | | | | | 775 | | | | | 780 | | |
| | | | | | | | | | | | | | | | | | |
| | CTT | ACT | GGG | TTC | AAG | ATG | CAT | GCC | CGG | GGT | TGG | ATA | TÇG | ATC | TAC | TGC | 2461 |
| | Leu | Thr | Gly | Phe | Lys | Met | His | Ala | Arg | Gly | Trp | Ile | Ser | Ile | Tyr | Сув | |
| | | | | 785 | | | | | 790 | | | | | 795 | | | |

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| | AAT | CCT | ÇCA | CGC | ССТ | GCG | TTC | AAG | GGA | TCT | GCA | CCA | ATC | TAA | CTT | TCT | 2509 |
|----|-------|-----|-------------|-----|------|-----|-----|-------------|-----|------|------|-----|------|-----|-----|------------------|------|
| | Asn | Pro | Pro | Arg | Pro | Ala | Phe | Lys | Gly | Ser | Ala | Pro | Ile | Asn | Leu | Ser | |
| | | | 800 | | | | | 805 | | | | | 810 | | | | |
| | _ | | | | | | | | | | | | | | | | |
| - | 5 GAT | CGT | TTG | AAC | CAA | GTT | CTT | CGA | TGG | GCT | TTG | GGA | TCT | ATC | GAG | ATT | 2557 |
| | Asp | Arg | Leu | Asn | Gln | Val | Leu | Arg | Trp | Ala | Leu | Gly | Ser | Ile | Glu | Ile | |
| | | 815 | | | | | 820 | | | | | 825 | | | | | |
| | | | | | | | | | | | | | | | | | |
| 17 | _ | CTT | | | | | | | | | | | | | | | 2605 |
| 11 |) Leu | Leu | Ser | Arg | H16 | - | Pro | He | Trp | Tyr | - | Tyr | His | GIY | Arg | | |
| | 830 | | | | | 835 | | | | | 840 | | | | | 845 | |
| | אכא | CTT | ምም ር | CAC | ACC. | እጥሮ | CCT | ጥ ልጥ | ልጥሮ | AAC | እሮሮ | ልጥሮ | GTC | ጥልጥ | رکس | እ ጥ ጥ | 2653 |
| | | Leu | | | | | | | | | | | | | | | 2033 |
| 1: | _ | пеп | neu | Gru | 850 | 116 | VIC | 171 | 116 | 855 | **** | 110 | vai | | 860 | 110 | |
| • | , | | | | 0.50 | | | | | 0,55 | | | | | 000 | | |
| | ACA | TCC | ATC | ССТ | СТТ | ልጥፐ | GCG | ТАТ | тст | АТТ | СТТ | CCC | GCT | ттт | TGT | СТС | 2701 |
| | | Ser | | | | | | | | | | | | | | | 2.02 |
| | | - | | 865 | 200 | | | •,,• | 870 | | | | •••• | 875 | ٠,٠ | 202 | |
| 20 | 0 | | | | | | | | 0.0 | | | | | 0.5 | | | |
| | | ACC | GAC | AGA | TTC | ATC | ATA | CCC | GAG | ATA | AGC | AAC | TAC | GCG | AGT | ATT | 2749 |
| | | Thr | | | | | _ | | | | | | | _ | | | |
| | | | 880 | 3 | | | | 885 | | | | | 890 | | | | |
| | | | | | | | | | | | | | | | | | |
| 2: | 5 TGG | TTC | ATT | СТА | CTC | TTC | ATC | TCA | ATT | GCT | GTG | ACT | GGA | ATC | CTG | GAG | 2797 |
| | Trp | Phe | Ile | Leu | Leu | Phe | Ile | Ser | Ile | Ala | Val | Thr | Gly | Ile | Leu | Glu | |
| | | 895 | | | | | 900 | | | | | 905 | | | | | |
| | | | | | | | | | | | | | | | | | |
| | CTG | AGA | TGG | AGC | GGT | GTG | AGC | ATT | GAG | GAT | TGG | TGG | AGG | AAC | GAG | CAG | 2845 |
| 30 | 0 Leu | Arg | Trp | Ser | Gly | Val | Ser | Ile | Glu | Asp | Trp | Trp | Arg | Asn | Glu | Gln | |
| | 910 | | | | | 915 | | | | | 920 | | | | | 925 | |
| | | | | | | | | | | | | | | | | | |
| | TTC | TGG | GTC | ATT | GGT | GGC | ACA | TCC | GCC | CAT | CTT | TTT | GCT | GTC | TTC | CAA | 2893 |
| | Phe | Trp | Val | Ile | Gly | Gly | Thr | Ser | Ala | His | Leu | Phe | Ala | Val | Phe | Gln | |
| 3: | 5 | | | | 930 | | | | | 935 | | | | | 940 | | |
| | | | | | | | | | | | | | | | | | |
| | GGT | CTA | CTT | AAG | GTT | CTT | GCT | GGT | ATC | GAC | ACC | AAC | TTC | ACC | GTT | ACA | 2941 |
| | Gly | Leu | Leu | Lys | Val | Leu | Ala | Gly | Ile | qaA | Thr | Asn | Phe | Thr | Val | Thr | |
| | | | | 945 | | | | | 950 | | | | | 955 | | | |

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| | TCT | AAA | GCC | ACA | GAC | GAA | GAT | GGG | GAT | TTT | GCA | GAA | CTC | TAC | ATC | TTC | 2989 |
|----|------|--------|------------|-------|-------|----------|-------|--------------|-------|------|----------|------------|---------|-------|---------|-------------|------|
| | Ser | Lys | Ala | Thr | Asp | Glu | Asp | Gly | Asp | Phe | Ala | Glu | Leu | Tyr | Ile | Phe | |
| | | | 960 | | | | | 965 | | | | | 970 | | | | |
| 5 | | | | | | | | | | | | | | | | | |
| 5 | | | | | | CTC | | | | | | | | | | | 3037 |
| | rys | 975 | inr | Ala | Leu | Leu | 980 | Pro | Pro | Thr | Tnr | | Leu | Leu | Val | Asn | |
| | | 313 | | | | | 700 | | | | | 985 | | | | | |
| | CTC | ATA | GGC | ATT | GTG | GCT | GGT | GTC | тст | TAT | GCT | GTA | AAC | AGT | GGC | ተ ልሮ | 3085 |
| 10 | | | | | | Ala | | | | | | | | | | | 5005 |
| | 990 | | • | | | 995 | • | | | • | 1000 | | | | | 1005 | |
| | | | | | | | | | | | | | | | | | |
| | CAG | TCG | TGG | GGT | CCG | CTT | TTC | GGG | AAG | CTC | TTC | TTC | GCC | TTA | TGG | GTT | 3133 |
| | Gln | Ser | Trp | Gly | Pro | Leu | Phe | Gly | Lys | Leu | Phe | Phe | Ala | Leu | Trp | Val | |
| 15 | | | | | 1010 | ס | | | | 1019 | 5 | | | | 102 | 0 | |
| | | | | | | | | | | | | | | | | | |
| | ТТА | GCC | CAT | CTC | TAC | CCT | TTC | TTG | AAA | GGT | CTG | TTG | GGA | AGA | CAA | AAC | 3181 |
| | Ile | Ala | His | | _ | Pro | Phe | Leu | - | - | Leu | Leu | Gly | Arg | Gln | Asn | |
| 20 | | | | 102 | 5 | | | | 103 | כ | | | | 103 | 5 | | |
| 20 | | | | | | | | | | | | | | | | | |
| | | | | | | GTC | | | | | | | | | | | 3229 |
| | AIG | 1111 | 104 | | 116 | Val | 116 | 104 | _ | 261 | .vai | reu | 105 | | ser | 116 | |
| | | | 201 | • | | | | 101. | | | | | 103 | | | | |
| 25 | TTC | TCG | TTG | CTT | TGG | GTC | AGG | ATC | AAT | CCC | TTT | GTG | GAC | GCC | AAT | CCC | 3277 |
| | | | | | | Val | | | | | | | | | | | |
| | | 105 | 5 | | • | | 1060 | 0 | | | | 1069 | 5 | | | | |
| | | | | | | | | | | | | | | | | | |
| | AAT | GCC | AAC | AAC | TTC | AAT | GGC | AAA | GGA | GGT | GTC | TTT | TAG | ACCC | TAT | | 3323 |
| 30 | Asn | Ala | Asn | Asn | Phe | Asn | Gly | Lys | Gly | Gly | Val | Phe | | | | | |
| | 107 | 0 | | | | 107 | 5 | | | | 108 | 0 , | | | | | |
| | | | | | | | | | | | | | | | | | |
| | TTA | TATA | CTT (| GTGT | GTGC | AT A | TATC | AAAA | A CG | CGCA | ATGG | GAA' | TTCC | AAA ' | TCAT | CTAAAC | 3383 |
| 26 | | | | | | | | | | | | | | | | | |
| 33 | CCA' | TCAA | ACC (| CCAG | TGAA | CC G | GGCA(| GTTA | A GG | TGAT | TCCA | TGT | CCAA | GAT ' | TAGC | TTTCTC | 3443 |
| | | am = = | | | | . | | | | a | . | m - | | | aa | D0000- | |
| | CGA | GTAG | CCA (| JAGA. | AGGT(| JA A | ATTG | TTCG' | ı AA | CACT | ATTG | TAA | IGAT | TT | CCAG | TGGGGA | 3503 |
| | ACN | ייעטע | י ביתנו | GACC | ימממי | ימ מיד | ימרמי | ተል ርጥ | ር ጥል፡ | מממר | ADGA | Δሞሞ | ተርሞተ | ነ ተጥ | الملحات | CTTATA | 3563 |
| 40 | | | . , | | | - | | | | | | 1 | | | | | 5505 |

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TTTATTTTAT TTAAAGCTTG TTAGACTCAC ACTTATGTAA TGTTGGAACT TGTTGTCCTA 3623 AAAAGGGATT GGAGTTTTCT TTTTATCTAA GAATCTGAAG TTTATATGCT 3673 5 (2) INFORMATION FOR SEQ ID NO:12: 10 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 1081 amino acids (B) TYPE: amino acid (D) TOPOLOGY: linear 15 (11) MOLECULE TYPE: protein (xi) SEQUENCE DESCRIPTION: SEQ ID NO:12: Met Glu Ala Ser Ala Gly Leu Val Ala Gly Ser Tyr Arg Arg Asn Glu 20 ı 10 15 Leu Val Arg Ile Arg His Glu Ser Asp Gly Gly Thr Lys Pro Leu Lys 25 20 30 25 Asn Met Asn Gly Gln Ile Cys Gln Ile Cys Gly Asp Asp Val Gly Leu Ala Glu Thr Gly Asp Val Phe Val Ala Cys Asn Glu Cys Ala Phe Pro 55 30 Val Cys Arg Pro Cys Tyr Glu Tyr Glu Arg Lys Asp Gly Thr Gln Cys 70 75 Cys Pro Gln Cys Lys Thr Arg Phe Arg Arg His Arg Gly Ser Pro Arg 35 85 90 Val Glu Gly Asp Glu Asp Glu Asp Asp Val Asp Asp Ile Glu Asn Glu

105

110

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| | Phe | Asn | - | Ala | Gln | Gly | Ala | Asn 120 | Lys | Ala | Arg | His | | Arg | His | Gly |
|----|-----|-----|-----|-----|-----|-----|-----|------------|-----|-----|-----|-----|-----|-----|-----|-----|
| | | | 115 | | | | | 120 | | | | | 125 | | | |
| | Glu | Glu | Phe | Ser | Ser | Ser | Ser | Arg | His | Glu | Ser | Gln | Pro | Ile | Pro | Leu |
| 5 | | 130 | | | | | 135 | | | | | 140 | | | | |
| | Leu | Thr | His | Gly | His | Thr | Val | Ser | Gly | Glu | Ile | Arg | Thr | Pro | Asp | Thr |
| | 145 | | | | | 150 | | | | | 155 | | | | | 160 |
| 10 | Gln | Ser | Val | Arg | Thr | Thr | Ser | Gly | Pro | Leu | Gly | Pro | Ser | Asp | Arg | Aen |
| | | | | | 165 | | | | | 170 | | | | | 175 | |
| | Ala | Ile | Ser | | Pro | Tyr | Ile | Asp | | Arg | Gln | Pro | Val | | Val | Arg |
| 15 | | | | 180 | | | | | 185 | | | | | 190 | | |
| | Ile | Val | Asp | Pro | Ser | Lys | Asp | Leu | Asn | Ser | Tyr | Gly | Leu | Gly | Asn | Val |
| | | | 195 | | | | | 200 | | | | | 205 | | | |
| 20 | Asp | - | Lys | Glu | Arg | Val | | Gly | Trp | Lys | Leu | Lys | Gln | Glu | Lys | Asn |
| 20 | | 210 | | | | | 215 | | | | | 220 | | | | |
| | Met | Leu | Gln | Met | Thr | Gly | Lys | Tyr | His | Glu | Gly | Lys | Gly | Gly | Glu | Ile |
| | 225 | | | | | 230 | | | | | 235 | | | | | 240 |
| 25 | Glu | Gly | Thr | Gly | Ser | Asn | Gly | Glu | Glu | Leu | Gln | Met | Ala | Asp | Авр | Thr |
| | | | | | 245 | | | | | 250 | | | | | 255 | |
| | Arg | Leu | Pro | Met | Ser | Arg | Val | Val | Pro | Ile | Pro | Ser | Ser | Arg | Leu | Thr |
| 30 | | | | 260 | | | | | 265 | | | | | 270 | | |
| | Pro | Tyr | Arg | Val | Val | Ile | Ile | Leu | Arg | Leu | Ile | Ile | Leu | Сув | Phe | Phe |
| | | | 275 | | | | | 280 | | | | | 285 | | | |
| | Leu | Gln | Tyr | Arg | Thr | Thr | His | Pro | Val | Lys | Asn | Ala | Tyr | Pro | Leu | Trp |
| 35 | | 290 | | | | | 295 | | | | | 300 | | | | |
| | Leu | Thr | Ser | Val | Ile | Сув | Glu | Ile | Trp | Phe | Ala | Phe | Ser | Trp | Leu | Leu |
| | 305 | | | | | 310 | | | | | 315 | | | | | 320 |

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| | Asp | Gln | Phe | Pro | Lys | Trp | Tyr | Pro | Ile | Asn | Arg | Glu | Thr | Tyr | Leu | Asp |
|----|------|------------|------------|------------|------|-----------|---------|------------|------|-----|------------|-----|------------|-----|-------|-------------|
| | | | | | 325 | | | | | 330 | | | | | 335 | |
| | | | | | | | | | | | | | | | | |
| | Ara | T.e.11 | Δla | Ile | Ara | ጥረድ | Δen | Ara | Agn | Glv | Glu | Pro | Sar | Gln | 1.011 | V=1 |
| 5 | A. g | Dea | | | n. y | - 7 - | nsp | ~-3 | _ | o. | JIU | | 561 | | Deu | V 41 |
| , | | | | 340 | | | | | 345 | | | | | 350 | | |
| | | | | | | | | | | | | | | | | |
| | Pro | Val | Asp | Val | Phe | Val | Ser | Thr | Val | Asp | Pro | Leu | Lys | Glu | Pro | Pro |
| | | | 355 | | | | | 360 | | | | | 365 | | | |
| | | | | | | | | | | | | | | | | |
| 10 | Leu | Val | Thr | Ala | Δgn | Thr | Val | t.eu | Ser | Tle | t.e.u | Ser | Val | Acn | Tyr | Pro |
| •• | Deu | | | 7,20 | 7.5 | | | | - | *** | | | 741 | nop | .,. | |
| | | 370 | | | | | 375 | | | | | 380 | | | | |
| | | | | | | | | | | | | | | | | |
| | Val | Asp | Lys | Val | Ala | Сув | Tyr | Val | Ser | Asp | qaA | Gly | Ser | Ala | Met | Leu |
| | 385 | | | | | 390 | | | | | 395 | | | | | 400 |
| 15 | | | | | | | | | | | | | | | | |
| | Thr | Phe | Glu | Ser | Leu | Ser | Glu | Thr | Ala | Glu | Phe | Ala | Lvs | Lvs | Trp | Val |
| | | | | | 405 | | | | • | 410 | | | -,- | -,- | 415 | |
| | | | | | 405 | | | | | 410 | | | | | 413 | |
| | | | | | | | | | | | | | | | | |
| | Pro | Phe | Cys | Lys | Lys | Phe | Asn | Ile | Glu | Pro | Arg | Ala | Pro | Glu | Phe | Tyr |
| 20 | | | | 420 | | | | | 425 | | | | | 430 | | |
| | | | | | | | | | | | | | | | | |
| | Phe | Ala | Gln | Lys | Ile | Asp | Tyr | Leu | Lys | Asp | Lys | Ile | Gln | Pro | Ser | Phe |
| | | | 435 | _ | | _ | _ | 440 | - | • | • | | 445 | | | |
| | | | | | | | | | | | | | ••• | | | |
| 25 | | | | | | | | | | | | | | | | |
| 23 | Val | Lys | Glu | Arg | Arg | Ala | Met | Lys | Arg | Glu | Tyr | Glu | Glu | Phe | Lys | Val |
| | | 450 | | | | | 455 | | | | | 460 | | | | |
| | | | | | | | | | | | | | | | | |
| | Arg | Ile | Asn | Ala | Leu | Val | Ala | Lys | Ala | Gln | Lys | Ile | Pro | Glu | Glu | Gly |
| | 465 | | | | | 470 | | | | | 475 | | | | | 480 |
| 30 | | | | | | | | | | | | | | | | |
| 50 | | 6 0 | | ~ 1 | | 63 | | | | _ | | _ | | | _ | _ |
| | Trp | Inr | mec | Gln | | GIY | inr | Pro | тър | | GIY | Asn | Asn | Inr | | Aab |
| | | | | | 485 | | | | | 490 | | | | | 495 | |
| | | | | | | | | | | | | | | | | |
| | His | Pro | Gly | Met | Ile | Gln | Val | Phe | Leu | Gly | His | Ser | Gly | Gly | Leu | qeA |
| 35 | | | | 500 | | | | | 505 | | | | | 510 | | |
| | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | |
| | Th~ | Ac= | Glv. | D.c.∞ | GJ | Lov | Dwa | A === | ī.ev | T)_ | The second | v-1 | C | A | C1 | T |
| | Thr | Asp | Gly 515 | Asn | Glu | Leu | Pro | Arg 520 | Leu | Ile | Tyr | Val | Ser 525 | Arg | Glu | Lys |

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| | Arg | Pro | Gly | Phe | Gln | His | His | Lys | Lys | Ala | Gly | Ala | Met | naA | Ala | Leu |
|----|------------|------------|-----------|---------|-------|----------|-------------|------|-------------|------------|-----|-----|------|------|-------------|-----|
| | | 530 | | | | | 535 | | | | | 540 | | | | |
| | | | | | | | | | | | | | | | | |
| | Ile | Arg | Val | Ser | Val | Val | Leu | Thr | Asn | Gly | Ala | Tyr | Leu | Leu | Asn | Val |
| 5 | 545 | _ | | | | 550 | | | | _ | 555 | _ | | | | 560 |
| | | | | | | | | | | | | | | | | |
| | Acn | Ove. | A co | ui e | T) 17 | Dhe |) cn | Acn | Ser | Lve | בות | Tla | 1 | Glu | 7 J 6 | Mak |
| | лэр | Cys | vəħ | n15 | | FIIC | ASII | non | Ser | | nia | 116 | Lys | GIU | | Met |
| | | | | | 565 | | | | | 570 | | | | | 575 | |
| 10 | | | | | | | | | | | | | | | | |
| 10 | Cys | Phe | Met | Met | Asp | Pro | Ala | Ile | Gly | Lys | Lys | Сув | Сув | Tyr | Val | Gln |
| | | | | 580 | | | | | 585 | | | | | 590 | | |
| | | | | | | | | | | | | | | | | |
| | Phe | Pro | Gln | Arg | Phe | Asp | Gly | Ile | Asp | Leu | His | qaA | Arg | Tyr | Ala | Asn |
| | | | 595 | | | | | 600 | | | | | 605 | | | |
| 15 | | | | | | | | | | | | | | | | |
| | Arg | Asn | Ile | Val | Phe | Phe | Q BA | Ile | Asn | Met | Lys | Gly | Leu | Asp | Gly | Ile |
| | - | 610 | | | | | 615 | | | | - | 620 | | • | • | |
| | | | | | | | | | | | | | | | | |
| | Gln | Glv | Pro | Val | Tvr | Val | Glv | Thr | Glv | C∨s. | CVS | Phe | Agn | Arg | Gln | Δla |
| 20 | 625 | . , | | • | .,. | 630 | U., | •••• | U 1, | Cyo | 635 | | NOII | Ary | G111 | 640 |
| | 023 | | | | | 030 | | | | | 633 | | | | | 040 |
| | • • • • | | 01 | | • | D | | • | | a 1 | ۵١. | | | | _ | _ |
| | Leu | lyr | GIY | ıyr | | Pro | vai | ren | Thr | | GIU | Asp | Leu | Glu | | Asn |
| | | | | | 645 | | | | | 650 | | | | | 655 | |
| | | | | | | | | | | | | | | | | |
| 25 | Ile | Ile | Val | Lys | Ser | Сув | Сув | Gly | Ser | Arg | Lys | Lys | Gly | Lys | Ser | Ser |
| | | | | 660 | | | | | 665 | | | | | 670 | | |
| | | | | | | | | | | | | | | | | |
| | Lys | Lys | Tyr | Asn | Tyr | Glu | Lys | Arg | Arg | Gly | Ile | Asn | Arg | Ser | Asp | Ser |
| | | | 675 | | | | | 680 | | | | | 685 | | | |
| 30 | | | | | | | | | | | | | | | | |
| | Asn | Ala | Pro | Leu | Phe | Aan | Met | Glu | Asn | Tle | na4 | Glu | Glv | Phe | Glu | Glv |
| | | 690 | | 400 | | | 695 | | | | пор | | Cly | riic | GIU | Gry |
| | | 0,50 | | | | | 693 | | | | | 700 | | | | |
| | m : | | | | _ | _ | | _ | | _ | | _ | _ | | | _ |
| 25 | | Asp | Asp | Glu | Arg | | Ile | Leu | Met | Ser | | Arg | Ser | Val | Glu | Lys |
| 33 | 705 | | | | | 710 | | | | | 715 | | | | | 720 |
| | | | | | | | | | | | | | | | | |
| | Arg | Phe | Gly | Gln | Ser | Pro | Val | Phe | Ile | Ala | Ala | Thr | Phe | Met | Glu | Gln |
| | | | | | 725 | | | | | 730 | | | | | 735 | |

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| | Gly | Gly | Ile | Pro 740 | Pro | Thr | Thr | Asn | Pro 745 | Ala | Thr | Leu | Leu | Lys 750 | Glu | Ala |
|----|-----|-----|-----|------------|------------|-----|-----|-----|------------|------------|-----|-----|-----|------------|------------|-----|
| | | | | 740 | | | | | ,43 | | | | | ,50 | | |
| _ | Ile | Нів | | Ile | Ser | Cys | Gly | _ | Glu | Asp | Lys | Thr | | Trp | Gly | Lys |
| 5 | | | 755 | | | | | 760 | | | | | 765 | | | |
| | Glu | Ile | Gly | Trp | Ile | Tyr | Gly | Ser | Val | Thr | Glu | qaA | Ile | Leu | Thr | Gly |
| | | 770 | | | | | 775 | | | | | 780 | | | | |
| 10 | Phe | Lys | Met | His | Ala | Arg | Gly | Trp | Ile | Ser | Ile | Tyr | Сув | Asn | Pro | Pro |
| | 785 | | | | | 790 | | | | | 795 | - | | | | 800 |
| | Ara | Pro | Δla | Phe | Lve | Glv | Ser | Δla | Pro | Tle | Aan | Leu | Ser | Aan | Ara | Leu |
| | Arg | 710 | AIG | 71 | 805 | Gly | 561 | n.u | | 810 | A0 | Deu | Je. | nap | 815 | 200 |
| 15 | | | | | | | | | | | | | | | | |
| | Asn | Gln | Val | Leu 820 | Arg | Trp | Ala | Leu | Gly 825 | Ser | Ile | Glu | Ile | Leu 830 | Leu | Ser |
| | | | | 020 | | | | | | | | | | 030 | | |
| 20 | Arg | His | - | Pro | Ile | Trp | Tyr | - | Tyr | His | Gly | Arg | | Arg | Leu | Leu |
| 20 | | | 835 | | | | | 840 | | | | | 845 | | | |
| | Glu | Arg | Ile | Ala | Tyr | Ile | Asn | Thr | Ile | Val | Tyr | Pro | Ile | Thr | Ser | Ile |
| | | 850 | | | | | 855 | | | | | 860 | | | | |
| 25 | Pro | Leu | Ile | Ala | Tvr | Cvs | Ile | Leu | Pro | Ala | Phe | Cvs | Leu | Ile | Thr | Asp |
| | 865 | | | | -,- | 870 | | | | | 875 | -,- | | | | 880 |
| | | | | _ | | | | | | | | | | | | _ |
| | Arg | Phe | Ile | Ile | Pro 885 | Glu | Ile | Ser | Ren | Tyr 890 | Ala | Ser | Ile | Trp | Phe 895 | Ile |
| 30 | | | | | | | | | | | | | | | | |
| | Leu | Leu | Phe | Ile | Ser | Ile | Ala | Val | | Gly | Ile | Leu | Glu | | Arg | Trp |
| | | | | 900 | | | | | 905 | | | | | 910 | | |
| | Ser | Gly | Val | Ser | Ile | Glu | Asp | Trp | Trp | Arg | Asn | Glu | Gln | Phe | Trp | Val |
| 35 | | | 915 | | | | | 920 | | | | | 925 | | | |
| | Ile | Glv | Glv | Thr | Ser | Ala | His | Leu | Phe | Ala | Val | Phe | Gln | Glv | Leu | Leu |
| | | 930 | • | | | | 935 | | | | | 940 | | 4 | | |
| | | | | | | | | | | | | | | | | |

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Lys Val Leu Ala Gly Ile Asp Thr Asn Phe Thr Val Thr Ser Lys Ala 945 950 955 960

Thr Asp Glu Asp Gly Asp Phe Ala Glu Leu Tyr Ile Phe Lys Trp Thr 5 965 970 975

Ala Leu Leu Ile Pro Pro Thr Thr Val Leu Leu Val Asn Leu Ile Gly 980 985 990

10 Ile Val Ala Gly Val Ser Tyr Ala Val Asn Ser Gly Tyr Gln Ser Trp
995 1000 1005

Gly Pro Leu Phe Gly Lys Leu Phe Phe Ala Leu Trp Val Ile Ala His 1010 1015 1020

15

Leu Tyr Pro Phe Leu Lys Gly Leu Leu Gly Arg Gln Asn Arg Thr Pro 1025 1030 1035 1040

Thr Ile Val Ile Val Trp Ser Val Leu Leu Ala Ser Ile Phe Ser Leu 20 1045 1050 1055

Leu Trp Val Arg Ile Asn Pro Phe Val Asp Ala Asn Pro Asn Ala Asn
1060 1065 1070

25 Asn Phe Asn Gly Lys Gly Gly Val Phe 1075 1080

- 30 (2) INFORMATION FOR SEQ ID NO:13:
 - (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1741 base pairs

(B) TYPE: nucleic acid

35 (C) STRANDEDNESS: single

(D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: cDNA
- 40 (iii) HYPOTHETICAL: NO

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| | | (iv | AN' | ΓI-SI | ENSE | : NO | | | | | | | | | | | |
|-----|-----|-------|----------|----------------|-----------|-------|---------|--------------|-------|-------|-------|-----|------|-----|------|-------|--------|
| | | (vi |) OR: | IGIN) A) OI | | | | za s | ativ | a | | | | | | | |
| 5 | | | | ., 0. | ·Orai | | OL y | 2 u 5 | | • | | | | | | | |
| | | (V11) | imi i | MEDIA | ATE S | SOUR | CE: | | | | | | | | | | |
| | | | (1 | B) C1 | LONE | : SO | 542 | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | |
| | | (ix |) FE | ATURI | Ξ: | | | | | | | | | | | | |
| 10 | | | (2 | A) N | AME/I | KEY: | CDS | | | | | | | | | | |
| | | | (1 | B) L(| CAT | ON: | 101 | 17 | 41 | | | | | | | | |
| | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | |
| 1.6 | | (xi |) SE(| QUEN | CE DI | ESCR: | IPTI | ON: | SEQ : | ID N | 0:13 | : | | | | | |
| 15 | | | | | | | | | | | | | | | | | |
| | GTG | JGGC | CGC (| .GCG(| CATC. | ra G | 3CTT | SCCG | C GC | GCGC | 3CGG | ATC | rucu | AGC | 1GCG | TAGCO | 60 |
| | ጥጥጥ | רדרכו | ייים ייי | ויני אניי | ויכים אינ | 2G D(| C A C (| ZAGG: | a ac | GGAG | BACC | ATG | ccc | GCG | אמר | GCG | 115 |
| | ••• | -100 | | ONO | | JU A | | 07100 | | 00110 | J1.00 | | | | Asn | | |
| 20 | | | | | | | | | | | | 1 | | | | 5 | |
| | | | | | | | | | | | | | | | | | |
| | GGG | ATG | GTG | GCG | GGA | TCC | CGC | AAC | CGG | AAC | GAG | TTC | GTC | ATG | ATC | CGC | 163 |
| | Gly | Met | Val | Ala | Gly | Ser | Arg | Asn | Arg | Asn | Glu | Phe | Val | Met | Ile | Arg | |
| | | | | | 10 | | | | | 15 | | | | | 20 | | |
| 25 | | | | | | | | | | | | | | | | | |
| | CCC | GAC | GGC | GAC | GCG | CCA | CCG | CCC | GCT | AAG | CCA | GGG | AAG | AGT | GTG | AAT | 211 |
| | Pro | Asp | Gly | Asp | Ala | Pro | Pro | Pro | Ala | Lys | Pro | Gly | Lys | Ser | Val | Asn | |
| | | | | 25 | | | | | 30 | | | | | 35 | | | |
| 30 | 000 | ~~~ | | | | | | | | | | | | | | | |
| 30 | GGT | | | | | | | | | | | | | | | | 259 |
| | GIY | GIII | 40 | Cys | GIII | 116 | Сув | 45 | дам | Thr | vaı | GIY | 50 | ser | Ald | Int | |
| | | | 10 | | | | | 43 | | | | | 30 | | | | |
| | GGC | GAC | GTC | ттт | GTT | GCC | TGC | AAT | GAG | TGC | GCC | TTC | CCG | GTC | TGC | CGC | 307 |
| 35 | Gly | | | | | | | | | | | | | | | | |
| | · | 55 | | | | | 60 | | | • | | 65 | | | • | - | |
| | | | | | | | | | | | | | | | | | |
| | CCT | TGC | TAC | GAG | TAC | GAA | CGC | AAG | GAA | GGG | AAC | CAG | TGC | TGC | ccc | CAG | 355 |
| | Pro | Cys | Tyr | Glu | Tyr | Glu | Arg | Lys | Glu | Gly | Asn | Gln | Суз | Cys | Pro | Gln | |
| 40 | 70 | | | | | 75 | | | | | 80 | | | | | 85 | |

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| | TGC | AAG | ACT | AGA | TAC | AAG | AGG | CAC | AAA | GGT | TGC | CCT | AGA | GTT | CAG | GGC | 403 |
|----|-----|-----|-----|-----|------------|-----|-----|-----|-----|-----|------|-----|-------|------|------|-------|-----|
| | Cys | Lys | Thr | Arg | Tyr | Lys | Arg | His | Lys | Gly | Cys | Pro | Arg | Val | Gln | Gly | |
| | | | | | 90 | | | | | 95 | | | | | 100 | | |
| _ | | | | | | | | | | | | | | | | | |
| 5 | GAT | | | | | | | | | | | | | | | | 451 |
| | Asp | Glu | Glu | | Glu | Asp | Val | Asp | _ | Leu | Asp | Asn | Glu | | His | Tyr | |
| | | | | 105 | | | | | 110 | | | | | 115 | | | |
| | | | | | 000 | | | 201 | 222 | maa | ~~ | | ~~ | | | | |
| 10 | Lys | | | | | | | | | | CAG | | | | | | 499 |
| 10 | Lys | RIS | 120 | Asn | GIY | гув | GIY | 125 | GIU | пр | GIII | 116 | 130 | Arg | GIN | GIY | |
| | | | 120 | | | | | 123 | | | | | 130 | | | | |
| | GAA | GAT | GTT | GAC | CTG | тст | TCA | тст | TCT | CGC | CAC | GAA | CAA | CAT | CGG | ATT | 547 |
| | | | | | | | | | | | His | _ | | | | _ | |
| 15 | | 135 | | • | | | 140 | | | • | | 145 | | | | | |
| | | | | | | | | | | | | | | | | | |
| | ccc | CGT | CTG | ACA | AGT | GGG | CAA | CAG | ATC | TCA | GGA | GAG | ATC | ССТ | GAT | GCT | 595 |
| | Pro | Arg | Leu | Thr | Ser | Gly | Gln | Gln | Ile | Ser | Gly | Glu | Ile | Pro | Asp | Ala | |
| | 150 | | | | | 155 | | | | | 160 | | | | | 165 | |
| 20 | | | | | | | | | | | | | | | | | |
| | TCC | CCC | GAT | CGC | CAT | TCT | ATC | CGC | AGC | GGA | ACA | TCA | AGC | TAT | GTT | GAT | 643 |
| | Ser | Pro | Asp | Arg | His | Ser | Ile | Arg | Ser | Gly | Thr | Ser | Ser | Tyr | Val | Asp | |
| | | | | | 170 | | | | | 175 | | | | | 180 | | |
| | | | | | | | | | | | | | | | | | |
| 25 | CCA | AGT | GTT | CCA | GTT | CCT | GTG | AGG | TTA | GTG | GAC | CCC | TCC | AAG | GAC | TTG | 691 |
| | Pro | Ser | Val | Pro | Val | Pro | Val | Arg | Ile | Val | Asp | Pro | Ser | Lys | Asp | Leu | |
| | | | | 185 | | | | | 190 | | | | | 195 | | | |
| | | | | | | | | | | | | | | | | | |
| 30 | | | | | | | | | | | CAA | | | | | | 739 |
| 30 | Asn | Ser | | GIY | 116 | Asn | Ser | | Asp | Trp | Gin | GIu | | Val | Ala | ser | |
| | | | 200 | | | | | 205 | | | | | 210 | | | | |
| | TCC | AGG | אאר | ממ | CAG | GAC | מממ | ልልጥ | ATG | ልጥር | CAG | СTA | C Cut | דממ | מממ | TAT | 787 |
| | | | | | | | | | | | | | | | | Tyr | 707 |
| 35 | | 215 | | 2,0 | 41. | nop | 220 | | | | 01 | 225 | ALG | ASII | Dy 3 | 7.7.1 | |
| | | 213 | | | | | 220 | | | | | 223 | | | | | |
| | CCA | GAG | GCA | AGA | GGG | GGA | GAC | ATG | GAA | GGG | ACT | GGT | TCA | AAT | GGT | GAA | 835 |
| | | | | | | | | | | | | | | | | Glu | |
| | 230 | | | _ | • | 235 | _ | | | • | 240 | - | | | -3 | 245 | |
| 40 | | | | | | | | | | | | | | | | · | |

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| | GAT | ATC | CAA | ATG | GTT | GAT | GAT | GCA | CGT | CTA | CCT | CTG | AGC | CGC | ATA | GTG | 883 |
|----|--------|-------|-----|-----|------|-----|--------|------|-------|---------|-----|-----|-------|-----|-------|-------|------|
| | Asp | Ile | Gln | Met | Val | Asp | Asp | Ala | Arg | Leu | Pro | Leu | Ser | Arg | Ile | Val | |
| | | | | | 250 | | | | | 255 | | | | | 260 | | |
| | | | | | | | | | | | | | | | | | |
| 5 | CCT | ATC | CCT | TCA | AAC | CAG | CTC | AAC | CTT | TAC | CGG | ATT | GTT | ATC | ATT | CTC | 931 |
| | Pro | Ile | Pro | Ser | Asn | Gln | Leu | Asn | Leu | Tyr | Arg | Ile | Val | Ile | Ile | Leu | |
| | | | | 265 | | | | | 270 | | | | | 275 | | | |
| | | | | | | | | | | | | | | | | | |
| | CGT | CTT | ATC | ATC | CTG | ATG | TTC | TTC | TTC | CAA | TAT | CGT | GTC | ACT | CAT | CCA | 979 |
| 10 | Arg | Leu | Ile | Ile | Leu | Met | Phe | Phe | Phe | Gln | Tyr | Arg | Val | Thr | His | Pro | |
| | | | 280 | | | | | 285 | | | | | 290 | | | | |
| | | | | | | | | | | | | | | | | | |
| | GTG | CGG | GAT | GCT | TAT | GGA | TTG | TGG | CTA | GTA | TCT | GTT | ATC | TGT | GAA | TTA | 1027 |
| | Val | Arg | qeA | Ala | Tyr | Gly | Leu | Trp | Leu | Val | Ser | Val | Ile | Cys | Glu | Ile | |
| 15 | | 295 | | | | | 300 | | | | | 305 | | | | | |
| | | | | | | | | | | | | | | | | | |
| | TGG | TTG | CCC | TTA | TCC | TGG | CTC | CTA | GAT | CAA | TTC | CCA | AAG | TGG | TAC | CCG | 1075 |
| | Trp | Leu | Pro | Leu | Ser | Trp | Leu | Leu | Asp | Gln | Phe | Pro | Lys | Trp | Tyr | Pro | |
| | 310 | | | | | 315 | | | | | 320 | | | | | 325 | |
| 20 | | | | | | | | | | | | | | | | | |
| | | | | GAA | | | | | | | | | | | | | 1123 |
| | Ile | Asn | Arg | Glu | | Tyr | Leu | Asp | Arg | | Ala | Leu | Arg | Tyr | _ | Arg | |
| | | | | | 330 | | | | | 335 | | | | | 340 | | |
| 25 | | | | | | | | | | | | | | | | | |
| 25 | | | | CCA | | | | | | | | | | | | | 1171 |
| | Glu | Gly | Glu | Pro | Ser | Gln | Leu | Ala | | Ile | Asp | Val | Phe | | Ser | Thr | |
| | | | | 345 | | | | | 350 | | | | | 355 | | | |
| | | | | | | | | | | | | | | | | | |
| 20 | | | | CTA | | | | | | | | | | | | | 1219 |
| 30 | Val | Asp | | Leu | Lys | Glu | Pro | | Leu | Ile | Thr | Ala | | Thr | Val | Leu | |
| | | | 360 | | | | | 365 | | | | | 370 | | | | |
| | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | GTT | 1267 |
| 25 | Ser | | Leu | Ala | Val | Asp | _ | Pro | Val | Asp | Lys | | Ser | Сув | Tyr | Val | |
| 35 | | 375 | | | | | 380 | | | | | 385 | | | | | |
| | Tr.Car | C 2 C | CAM | CCT | mar. | CCm | א שערו | mm s | N Com | eponer. | CAC | COT | Catho | ጥጣኦ | C 2 2 | N CTT | 1215 |
| | | | | GGT | | | | | | | | | | | | | 1315 |
| | | чар | чар | Gly | ser | | Met | ren | Inr | rne | | WIS | ₽€ſſ | ser | GIU | | |
| 40 | 390 | | | | | 395 | | | | | 400 | | | | | 405 | |
| 10 | | | | | | | | | | | | | | | | | |

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| | GCA | GAA | TTT | GCT | AGG | AAG | TGG | GTT | CCG | TTT | TGC | AAG | AAG | CAC | AAT | ATT | 1363 |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|-----|------|-----|------|-----|------|
| | Ala | Glu | Phe | Ala | Arg | Lys | Trp | Val | Pro | Phe | Cys | Lys | Lys | His | Asn | Ile | |
| | | | | | 410 | | | | | 415 | | | | | 420 | | |
| | | | | | | | | | | | | | | | | | |
| 5 | GAA | CCA | CGA | GCT | CCA | GAG | TTT | TAC | TTT | GCT | CAA | AAA | ATA | GAT | TAC | CTG | 1411 |
| | Glu | Pro | Arg | Ala | Pro | Glu | Phe | Tyr | Phe | Ala | Gln | Lys | Ile | Asp | Tyr | Leu | |
| | | | | 425 | | | | | 430 | | | | | 435 | | | |
| | | | | | | | | | | | | | | | | | |
| | | | | | CAA | | | | | | | | | | | | 1459 |
| 10 | Lys | yab | | Ile | Gln | Pro | Ser | | Val | Lys | Glu | Arg | | Ala | Met | Lys | |
| | | | 440 | | | | | 445 | | | | | 450 | | | | |
| | | | | | | | | | | | | | | | | | |
| | | | | | GAA | | | | | | | | | | | | 1507 |
| 15 | Arg | | Tyr | GIU | Glu | Pne | | vaı | Arg | He | Asn | | Leu | vai | Ala | Lya | |
| 13 | | 455 | | | | | 460 | | | | | 465 | | | | | |
| | GCA | 447 | ΔΔΔ | ата | CCT | CAD | GAG | GGG | TGG | ACC | ልተሃር | CCT | ርልጥ | GGC | ልሮሞ | CCT | 1555 |
| | | | | | Pro | | | | | | | | | | | | 1333 |
| | 470 | | -1- | | | 475 | | , | | | 480 | | ,,op | 01, | •••• | 485 | |
| 20 | | | | | | | | | | | | | | | | | |
| | TGG | ССТ | GGG | AAT | AAC | CCA | AGG | GAT | CAC | CCT | GGC | ATG | ATT | CAG | GTG | TTC | 1603 |
| | Trp | Pro | Gly | Asn | Asn | Pro | Arg | Авр | His | Pro | Gly | Met | Ile | Gln | Val | Phe | |
| | | | | | 490 | | | | | 495 | | | | | 500 | | |
| | | | | | | | | | | | | | | | | | |
| 25 | TTG | GGG | CAC | AGT | GGT | GGG | CTT | GAC | ACT | GAT | GGT | AAC | GAG | TTG | CCA | CGG | 1651 |
| | Leu | Gly | His | Ser | Gly | Gly | Leu | Asp | Thr | Asp | Gly | Asn | Glu | Leu | Pro | Arg | |
| | | | | 505 | | | | | 510 | | | | | 515 | | | |
| | | | | | | | | | | | | | | | | | |
| | CTT | GTC | TAC | GTC | TCT | CGT | GAA | AAG | AGG | CCA | GGA | TTC | CAG | CAT | CAC | AAG | 1699 |
| 30 | Leu | Val | Tyr | Val | Ser | Arg | Glu | Lys | Arg | Pro | Gly | Phe | Gln | His | His | Lys | |
| | | | 520 | | | | | 525 | | | | | 530 | | | | |
| | | | | | | | | | | | | | | | | | |
| | AAG | GCT | GGT | GCA | ATG | AAT | GCA | TTG | ATT | CGT | GTA | TCT | GCT | GTG | | | 1741 |
| 2.5 | Lys | | Gly | Ala | Met | Asn | | Leu | Ile | Arg | Val | | Ala | Val | | | |
| 35 | | 535 | | | | | 540 | | | | | 545 | | | | | |

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| | (2) | INF | ORMA: | rion | FOR | SEQ | ID I | NO:14 | 1 : | | | | | | | |
|----|-----|-------|-------|-------|-------|-------|---------------|--------|------------|-------|-------|--------|-----|-----|------|-----|
| | | | (i) ! | SEQUI | ENCE | CHAI | RACTI | ERIST | rics: | : | | | | | | |
| | | | | (A) | LE | NGTH: | 54 | 7 ami | ino a | acids | 3 | | | | | |
| 5 | | | | | | PE: a | | | | | | | | | | |
| , | | | | • | | - | | | | | | | | | | |
| | | | | (D) | 101 | POLO | 31 : . | Linea | a r | | | | | | | |
| | | (: | i) l | MOLEC | TULE | TYPI | E: p | rote | in | | | | | | | |
| 10 | | (; | ki) (| SEQUI | ENCE | DESC | CRIP | rion : | : SE(| Q ID | NO: 3 | 14: | | | | |
| | Met | Ala | Ala | Asn | Ala | Gly | Met | Val | Ala | Gly | Ser | Arg | Asn | Arg | Asn | Glu |
| | 1 | | | | 5 | | | | | 10 | | | | | 15 | |
| | | | | | | | | | | | | | | | | |
| 15 | Phe | Val | Met | Ile | Arg | Pro | Asp | Gly | Asp | Ala | Pro | Pro | Pro | Ala | Lys | Pro |
| | | | | 20 | | | | | 25 | | | | | 30 | | |
| | | | | | | | | | | | | | | | | |
| | Glv | Lvs | Ser | Val | Agn | Glv | Gln | Val | Cvs | Gln | Tle | Cvs | Glv | Asn | Thr | Val |
| | 0-7 | 2,0 | 35 | | -1011 | 01, | | 40 | 0,70 | | | 0,0 | 45 | | •••• | |
| 20 | | | 33 | | | | | 40 | | | | | 413 | | | |
| 20 | | | | | | | | | | | | | _ | | _ | |
| | Gly | Val | Ser | Ala | Thr | Gly | Asp | Val | Phe | Val | Ala | Сув | Asn | Glu | Сув | Ala |
| | | 50 | | | | | 55 | | | | | 60 | | | | |
| | | | | | | | | | | | | | | | | |
| | Phe | Pro | Val | Cys | Arg | Pro | Сув | Tyr | Glu | Tyr | Glu | Arg | Lys | Glu | Gly | Asn |
| 25 | 65 | | | | | 70 | | | | | 75 | | | | | 80 |
| | | | | | | | | | | | | | | | | |
| | Gln | Cys | Cys | Pro | Gln | Cys | Lys | Thr | Arg | Tyr | Lys | Arg | His | Lys | Gly | Cys |
| | | _ | _ | | 85 | _ | _ | | | 90 | _ | _ | | _ | 95 | _ |
| | | | | | | | | | | | | | | | | |
| 30 | Pro | Ara | Val | Gln | Glv | Agn | Glu | Glu | Glu | G1 v | Δan | Val | Agn | Acn | Len | Aen |
| | | *** 3 | , | 100 | CI | nop | 014 | | 105 | 014 | пор | V 44 1 | nop | | Deu | лор |
| | | | | 100 | | | | | 103 | | | | | 110 | | |
| | | | | | _ | | | | | | | | | | | _ |
| | Asn | Glu | Phe | His | Tyr | Lys | His | Gly | Asn | Gly | Lys | Gly | Pro | Glu | Trp | Gln |
| | | | 115 | | | | | 120 | | | | | 125 | | | |
| 35 | | | | | | | | | | | | | | | | |
| | Ile | Gln | Arg | Gln | Gly | Glu | Asp | Val | Asp | Leu | Ser | Ser | Ser | Ser | Arg | His |
| | | 130 | | | | | 135 | | | | | 140 | | | | |
| | | | | | | | | | | | | | | | | |
| | Glu | Gln | His | Arg | Ile | Pro | Arg | Leu | Thr | Ser | Gly | Gln | Gln | Ile | Ser | Gly |
| 40 | 145 | | | _ | | 150 | _ | | | | 155 | | | | | 160 |
| | | | | | | | | | | | | | | | | |

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| | Glu | Ile | Pro | Asp | Ala 165 | Ser | Pro | Asp | Arg | His 170 | Ser | Ile | Arg | Ser | Gly 175 | Thr |
|----|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| 5 | Ser | Ser | Tyr | Val 180 | Asp | Pro | Ser | Val | Pro 185 | Val | Pro | Val | Arg | Ile 190 | Val | Asp |
| | Pro | Ser | Lув 195 | Asp | Leu | Asn | Ser | Tyr 200 | Gly | Ile | Asn | Ser | Val 205 | Ąap | Trp | Gln |
| 10 | Glu | Arg 210 | Val | Ala | Ser | Trp | Arg 215 | Asn | ŗåa | Gln | qaA | Lys 220 | Asn | Met | Met | Gln |
| 15 | Val 225 | Ala | Asn | Lys | Tyr | Pro 230 | Glu | Ala | Arg | Gly | Gly 235 | Asp | Met | Glu | Gly | Thr 240 |
| | Gly | Ser | Asn | Gly | Glu 245 | Авр | Ile | Gln | Met | Val 250 | Asp | Asp | Ala | Arg | Leu 255 | Pro |
| 20 | Leu | Ser | Arg | Ile 260 | Val | Pro | Ile | Pro | Ser 265 | Asn | Gln | Leu | Asn | Leu 270 | Tyr | Arg |
| | Ile | Val | 11e 275 | Ile | Leu | Arg | Leu | 11e 280 | Ile | Leu | Met | Phe | Phe 285 | Phe | Gln | Tyr |
| 25 | Arg | Val 290 | Thr | His | Pro | Val | Arg 295 | Asp | Ala | Tyr | Gly | Leu 300 | Trp | Leu | Val | Ser |
| 30 | Val 305 | Ile | Сув | Glu | Ile | Trp 310 | Leu | Pro | Leu | Ser | Trp 315 | Leu | Leu | Asp | Gln | Phe |
| | Pro | Lya | Trp | Tyr | Pro 325 | Ile | Asn | Arg | Glu | Thr 330 | Tyr | Leu | Asp | Arg | Leu 335 | Ala |
| 35 | Leu | Arg | Tyr | Asp 340 | Arg | Glu | Gly | Glu | Pro 345 | Ser | Gln | Leu | Ala | Pro 350 | Ile | Asp |
| | Val | Phe | Val 355 | Ser | Thr | Val | Asp | Pro 360 | Leu | Lys | Glu | Pro | Pro 365 | | Ile | Thr |

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| | Ala | Asn | Thr | Val | Leu | Ser | Ile | Leu | Ala | Val | Asp | Tyr | Pro | Val | Asp | Lys |
|----|-------|------|------------------|------|------|------|-----|-----------|-------------|--------|-----|-----|------|-----|-----|-------------|
| | | 370 | | | | | 375 | | | | | 380 | | | | |
| | | | | | | | | | | | | | | | | |
| 5 | Val | Ser | Cvs | Tvr | Val | Ser | Asp | Asp | Glv | Ser | Ala | Met | Leu | Thr | Phe | Glu |
| • | 385 | | -7- | -,- | | 390 | | | • | | 395 | | | | | 400 |
| | 303 | | | | | 330 | | | | | ,,, | | | | | 100 |
| | | | | | | _ | | | | _ | _ | _ | | _ | | _ |
| | Ala | Leu | Ser | Glu | Thr | Ala | Glu | Phe | Ala | - | Lys | Trp | Val | Pro | | Cys |
| | | | | | 405 | | | | | 410 | | | | | 415 | |
| 10 | | | | | | | | | | | | | | | | |
| | Lys | Lys | His | Asn | Ile | Glu | Pro | Arg | Ala | Pro | Glu | Phe | Tyr | Phe | Ala | Gln |
| | | | | 420 | | | | | 425 | | | | | 430 | | |
| | | | | | | | | | | | | | | | | |
| | I.vg | tle | Asp | Tyr | Leu | Lvs | Asp | Lvs | Ile | Gln | Pro | Ser | Phe | Val | Lvs | Glu |
| 15 | -,- | | 435 | -7- | | -,- | | 440 | | | | | 445 | | • | |
| 13 | | | 433 | | | | | 440 | | | | | 443 | | | |
| | | | | | | | | | | | | _ | | _ | | |
| | Arg | Arg | Ala | Met | Lys | Arg | Glu | Tyr | Glu | Glu | Phe | Lys | Val | Arg | Ile | Asn |
| | | 450 | | | | | 455 | | | | | 460 | | | | |
| | | | | | | | | | | | | | | | | |
| 20 | Ala | Leu | Val | Ala | Lys | Ala | Gln | Lys | Val | Pro | Glu | Glu | Gly | Trp | Thr | Met |
| | 465 | | | | | 470 | | | | | 475 | | | | | 480 |
| | | | | | | | | | | | | | | | | |
| | a l A | Aen | Gly | Thr | Δla | Trn | Pro | Glv | Agn | Agn | Pro | Ara | Asn | His | Pro | Glv |
| | Aια | rap | O _z y | **** | 485 | | | 01 | | 490 | | ••• | ···· | | 495 | - _, |
| 25 | | | | | 465 | | | | | 430 | | | | | 425 | |
| 23 | | | | | | | | | | | | | | | | |
| | Met | Ile | Gln | Val | Phe | Leu | Gly | His | Ser | Gly | Gly | Leu | Asp | Thr | Asp | Gly |
| | | | | 500 | | | | | 505 | | | | | 510 | | |
| | | | | | | | | | | | | | | | | |
| | Asn | Glu | Leu | Pro | Arg | Leu | Val | Tyr | Val | Ser | Arg | Glu | Lys | Arg | Pro | Gly |
| 30 | | | 515 | | | | | 520 | | | | | 525 | | | |
| | | | | | | | | | | | | | | | | |
| | Dhe | G1 n | Hic | His | Lve | Late | ءاھ | G1v | פו ע | Met | Aan | Δls | Leu | Tle | Δνα | Val |
| | FIIC | | ***** | 4110 | -y a | _y a | | O+ y | viq | 1-10 C | YOU | | Tea | **6 | | +61 |
| | | 530 | | | | | 535 | | | | | 540 | | | | |
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| 35 | Ser | Ala | Val | | | | | | | | | | | | | |
| | 545 | | | | | | | | | | | | | | | |

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CLAIMS:

- An isolated nucleic acid molecule which encodes a polypeptide of the cellulose biosynthetic pathway or a homologue, analogue or derivative thereof or a complementary sequence thereto, wherein said polypeptide is capable of producing cellulose and/or β-1,4-5 glucan and/or an intermediate between cellulose and a β-1,4-glucan polymer.
 - 2. The isolated nucleic acid molecule according to claim 1 wherein the polypeptide is cellulose synthase or a catalytic subunit thereof.
- 10 3. The isolated nucleic acid molecule according to claim 1 or 2, derived from a prokaryote.
- The isolated nucleic acid molecule according to claim 3, wherein the prokaryote is a bacterium other than Agrobacterium tumefaciens. Acetobacter pasteurianus or Acetobacter
 xylinum.
 - 5. The isolated nucleic acid molecule according to claim 1 or 2, derived from a eukaryote.
- 20 6. The isolated nucleic acid molecule according to claim 5, wherein the eukaryote is a plant or fungus.
 - 7. The isolated nucleic acid molecule according to claim 6, wherein the plant is selected from the list comprising Arabidopsis thaliana, Gossypium hirsutum (cotton), Oryza sativa
- 25 (rice), wheat, barley, maize, Brassica ssp., Eucalyptus ssp., hemp, jute, flax, Pinus ssp., Populus ssp., and Picea spp., amongst others.
 - 8. The isolated nucleic acid molecule according to claim 2 wherein the cellulose synthase or catalytic subunit thereof is the *Arabidopsis thaliana* RSW1 polypeptide.

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9. The isolated nucleic acid molecule according to any one of claims 1 to 8. comprising a sequence of nucleotides which is at least 40% identical to any one of SEQ ID NOs:1, 3, 4, 5, 7, 9, 11 or 13 or a complementary sequence thereof.

- 10. The isolated nucleic acid molecule according to claim 9, wherein the percentage identity to any one of SEQ ID NOs:1, 3, 4, 5, 7, 9, 11 or 13 or a complementary sequence thereof is at least 60%.
- 10 11. The isolated nucleic acid molecule according to claim 9, wherein the percentage identity to any one of SEQ ID NOs:1, 3, 4, 5, 7, 9, 11 or 13 or a complementary sequence thereof is at least 80%.
- 12. An isolated nucleic acid molecule which comprises a sequence of nucleotides substantially as set forth in any one of SEQ ID NOs:3, 4, 5, 7, 9 or 11 or a homologue, analogue or derivative thereof or a complementary sequence thereto.
- 13. The isolated nucleic acid molecule according to any one of claims 1 to 12, wherein said nucleic acid molecule hybridizes under at least low stringency conditions to at least 20 contiguous nucleotides of any one of SEQ ID NOs:1, 3, 4, 5, 7, 9, 11 or 13 or a complementary sequence thereto.
- 14. An isolated nucleic acid molecule which encodes a polypeptide which is capable of cellulose and/or β-1,4- glucan biosynthesis in a plant cell, fungal cell, insect cell. animal cell,
 25 yeast cell or bacterial cell when expressed therein.
 - 15. The isolated nucleic acid molecule according to claim 14, wherein the polypeptide is cellulose synthase or a catalytic subunit thereof.
- 30 16. The isolated nucleic acid molecule according to claim 14 or 15, derived from a

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prokaryote.

- 17. The isolated nucleic acid molecule according to claim 16, wherein the prokaryote is a bacterium other than Agrobacterium tumefaciens, Acetobacter pasteurianus or Acetobacter 5 xylinum.
 - 18. The isolated nucleic acid molecule according to claim 14 or 15, derived from a eukaryote.
- 10 19. The isolated nucleic acid molecule according to claim 18, wherein the eukaryote is a plant or fungus.
- The isolated nucleic acid molecule according to claim 19, wherein the plant is selected from the list comprising Arabidopsis thaliana, Gossypium hirsutum (cotton), Oryza sativa
 (rice), wheat, barley, maize, Brassica ssp., Eucalyptus ssp., hemp, jute, flax, Pinus ssp., Populus ssp., and Picea spp., amongst others.
 - 21. The isolated nucleic acid molecule according to claim 20, wherein the cellulose synthase or catalytic subunit thereof is the *Arabidopsis thaliana* RSW1 polypeptide.

- 22. The isolated nucleic acid molecule according to any one of claims 14 to 21, comprising a sequence of nucleotides which is at least 40% identical to any one of SEQ ID NOs:1, 3, 4, 5, 7, 9, 11 or 13 or a complementary sequence thereto.
- 25 23. The isolated nucleic acid molecule according to claim 22, wherein the percentage identity to any one of SEQ ID NOs:1, 3, 4, 5, 7, 9, 11 or 13 or a complementary sequence thereof is at least 60%.
- 24. The isolated nucleic acid molecule according to claim 22, wherein the percentage 30 identity to any one of SEQ ID NOs:1, 3, 4, 5, 7, 9, 11 or 13 or a complementary sequence

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thereof is at least 80%.

- 25. The isolated nucleic acid molecule according to claim 22, comprising the sequence of nucleotides substantially as set forth in any one of SEQ ID NOs:3, 4, 5, 7, 9 or 11 or a 5 homologue, analogue or derivative thereof or a complementary sequence thereto.
- 26. An isolated nucleic acid molecule which encodes or is complementary to a nucleic acid molecule which encodes a polypeptide capable of cellulose and/or β-1,4-glucan biosynthesis wherein said polypeptide comprises a sequence of amino acids which is at least 10 40% identical to any one of SEQ ID Nos:2, 6, 8, 10, 12 or 14.
 - 27. The isolated nucleic acid molecule according to claim 26, wherein the percentage identity to any one of SEQ ID Nos:2, 6, 8, 10, 12 or 14 is at least 60%.
- 15 28. The isolated nucleic acid molecule according to claim 27, wherein the percentage identity to any one of SEQ ID Nos:2, 6, 8, 10, 12 or 14 is at least 80%.
- 29. The isolated nucleic acid molecule according to claim 26, wherein the polypeptide comprises a sequence of amino acids substantially as set forth in any one of SEQ ID Nos:2, 20 6, 8, 10, 12 or 14.
 - 30. A genetic construct which comprises the isolated nucleic acid molecule according to any one of claims 1 to 29.
- 25 31. A genetic construct which comprises the isolated nucleic acid molecule according to any one of claims 1 to 29 operably connected to a promoter sequence.
- 32. The genetic construct according to claim 31, wherein the nucleic acid molecule is operably connected to the promoter sequence in the sense orientation such that RNA which 30 encodes a polypeptide capable of cellulose and/or β-1,4-glucan biosynthesis or a homologue,

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analogue or derivative thereof is produced when said nucleic acid molecule is expressed.

- 33. The genetic construct according to claim 31, wherein the nucleic acid molecule is operably connected to the promoter sequence in the antisense orientation such that RNA which is complementary to RNA which encodes a polypeptide capable of cellulose and/or β-1,4-glucan biosynthesis or a homologue, analogue or derivative thereof, is produced when said nucleic acid molecule is expressed.
- 34. The genetic construct according to claim 33, wherein the nucleic acid molecule 10 encodes an antisense or ribozyme molecule.
 - 35. The genetic construct according to any one of claims 31 to 34, wherein the promoter is the CaMV 35S promoter.
- 15 36. The genetic construct according to any one of claims 31 to 34, wherein the promoter is the *Arabidopsis thaliana RSW*1 gene promoter.
- 37. A method of increasing the level of cellulose in a cell, tissue, organ or organism, said method comprising expressing the isolated nucleic acid molecule according to any one of 20 claims 1 to 29 therein, in the sense orientation, for a time and under conditions at least sufficient to produce or increase expression of the polypeptide encoded therefor.
 - 38. The method according to claim 37, comprising the additional first step of transforming the cell, tissue, organ or organism with the isolated nucleic acid molecule.
 - 39. The method according to claim 38, wherein the cell is a prokaryotic cell.
 - 40. The method according to claim 38, wherein the cell, tissue, organ or organism is a eukaryotic cell, tissue, organ or organism.

- 41. The method according to claim 40, wherein the cell, tissue, organ or organism is a plant, fungal, insect, animal or yeast cell, tissue, organ or organism.
- 42. The method according to claim 41, wherein the cell, tissue, organ or organism is a 5 plant cell, tissue, organ or organism.
- 43. The method according to claim 42 wherein the plant is selected from the list comprising Arabidopsis thaliana, Gossypium hirsutum (cotton), Oryza sativa (rice), Eucalyptus ssp., Brassica ssp., wheat, barley, maize, hemp, jute, flax, and woody plants 10 such as Pinus ssp., Populus ssp., Picea spp., amongst others.
- 44. A method of reducing the level of non-crystalline β-1,4-glucan in a cell, tissue, organ or organism, said method comprising expressing the isolated nucleic acid molecule according to any one of claims 1 to 29 therein, in the sense orientation, for a time and under conditions
 15 at least sufficient to produce or increase expression of the polypeptide encoded therefor.
 - 45. The method according to claim 44, comprising the additional first step of transforming the cell, tissue, organ or organism with the isolated nucleic acid molecule.
 - 46. The method according to claim 44, wherein the cell is a prokaryotic cell.

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- 47. The method according to claim 44, wherein the cell, tissue, organ or organism is a eukaryotic cell, tissue, organ or organism.
- 48. The method according to claim 47, wherein the cell, tissue, organ or organism is a plant, fungal, insect, animal or yeast cell, tissue, organ or organism.
- 49. The method according to claim 48, wherein the cell, tissue, organ or organism is a 30 plant cell, tissue, organ or organism.

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50. The method according to claim 50 wherein the plant is selected from the list comprising Arabidopsis thaliana, Gossypium hirsutum (cotton), Oryza sativa (rice), Eucalyptus ssp., Brassica ssp., wheat, barley, maize, hemp, jute, flax, and woody plants such as Pinus ssp., Populus ssp., Picea spp., amongst others.

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51. A method of reducing the level of starch in a cell, tissue, organ or organism, said method comprising expressing the isolated nucleic acid molecule according to any one of claims 1 to 29 therein, in the sense orientation, for a time and under conditions at least sufficient to produce or increase expression of the polypeptide encoded therefor.

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- 52. The method according to claim 50, comprising the additional first step of transforming the cell, tissue, organ or organism with the isolated nucleic acid molecule.
- 53. The method according to claim 51, wherein the cell is a prokaryotic cell.

- 54. The method according to claim 53, wherein the cell, tissue, organ or organism is a eukaryotic cell, tissue, organ or organism.
- 55. The method according to claim 54, wherein the eukaryote is a plant. fungus, insect, 20 animal or yeast.
 - 56. The method according to claim 55, wherein the eukaryote is a plant.
- 57. The method according to claim 56 wherein the plant is selected from the list comprising Arabidopsis thaliana, Gossypium hirsutum (cotton), Oryza sativa (rice), Eucalyptus ssp., Brassica ssp., wheat, barley, maize, hemp, jute, flax, and woody plants such as Pinus ssp., Populus ssp., Picea spp., amongst others.
- 58. A method of reducing the level of cellulose in a cell, tissue, organ or organism, said 30 method comprising expressing the isolated nucleic acid molecule according to any one of

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claims 1 to 29 therein, in the antisense orientation, for a time and under conditions at least sufficient to prevent or reduce the expression of the polypeptide encoded therefor.

- 59. The method according to claim 58, comprising the additional first step of transforming the cell, tissue, organ or organism with the isolated nucleic acid molecule.
 - 60. The method according to claims 58 or 59, wherein the cell, tissue, organ or organism is a eukaryotic cell, tissue, organ or organism.
- 10 61. The method according to claim 60, wherein the eukaryote is a plant, fungus, insect, animal or yeast.
 - 62. The method according to claim 61, wherein the eukaryote is a plant.
- 15 63. The method according to claim 62 wherein the plant is selected from the list comprising Arabidopsis thaliana, Gossypium hirsutum (cotton), Oryza sativa (rice), Eucalyptus ssp., Brassica ssp., wheat, barley, maize, hemp, jute, flax, and woody plants such as Pinus ssp., Populus ssp., Picea spp., amongst others.
- 20 64. A method of increasing the level of non-crystalline β-1,4-glucan in a cell, tissue, organ or organism, said method comprising expressing the isolated nucleic acid molecule according to any one of claims 1 to 29 therein, in the antisense orientation, for a time and under conditions at least sufficient to prevent or reduce the expression of the polypeptide encoded therefor.

- 65. The method according to claim 64, comprising the additional first step of transforming the cell, tissue, organ or organism with the isolated nucleic acid molecule.
- 66. The method according to claims 64 or 65, wherein the cell, tissue, organ or organism 30 is a eukaryotic cell, tissue, organ or organism.

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- 67. The method according to claim 66, wherein the eukaryote is a plant, fungus, insect, animal or yeast.
- 68. The method according to claim 67, wherein the eukaryote is a plant.

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69. The method according to claim 68 wherein the plant is selected from the list comprising Arabidopsis thaliana, Gossypium hirsutum (cotton), Oryza sativa (rice), Eucalyptus ssp., Brassica ssp., wheat, barley, maize, hemp, jute, flax, and woody plants such as Pinus ssp., Populus ssp., Picea spp., amongst others.

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70. A method of increasing the level of starch in a cell, tissue, organ or organism, said method comprising expressing the isolated nucleic acid molecule according to any one of claims 1 to 29 therein, in the antisense orientation, for a time and under conditions at least sufficient to prevent or reduce the expression of the polypeptide encoded therefor.

- 71. The method according to claim 70, comprising the additional first step of transforming the cell, tissue, organ or organism with the isolated nucleic acid molecule.
- 72. The method according to claims 70 or 71, wherein the cell, tissue, organ or organism 20 is a eukaryotic cell, tissue, organ or organism.
 - 73. The method according to claim 72, wherein the eukaryote is a plant, fungus, insect, animal or yeast.
- 25 74. The method according to claim 73, wherein the eukaryote is a plant.
- 75. The method according to claim 74 wherein the plant is selected from the list comprising Arabidopsis thaliana, Gossypium hirsutum (cotton), Oryza sativa (rice), Eucalyptus ssp., Brassica ssp., wheat, barley, maize, hemp, jute, flax, and woody plants 30 such as Pinus ssp., Populus ssp., Picea spp., amongst others.

- 76. A method of producing a recombinant enzymatically active polypeptide which is capable of synthesizing cellulose and/or β-1,4-glucan and/or an intermediate between cellulose and β-1,4-glucan in a cell, said method comprising expressing the isolated nucleic acid molecule according to any one of claims 1 to 29 or a homologue, analogue or derivative thereof in said cell for a time and under conditions sufficient for the polypeptide encoded therefor to be produced.
- 77. The method according to claim 76, comprising the additional first step of transforming the cell with the isolated nucleic acid molecule according to any one of claims 10 1 to 29 or the genetic construct according to any one of claims 11 to 15.
 - 78. A recombinant polypeptide produced according to the method defined by claim 76 or 77.
- 15 79. The recombinant cellulose biosynthetic polypeptide according to claim 78, further defined as a recombinant cellulose synthase or catalytically active subunit thereof.
- 80. A recombinant cellulose biosynthetic polypeptide capable of cellulose and/or β-1,4-glucan production and comprising a sequence of amino acids set forth in any one of SEQ ID
 20 Nos: 2, 6, 8, 10, 12 or 14 or a homologue, analogue or derivative thereof which is at least 40% identical thereto.
 - 81. The recombinant cellulose biosynthetic polypeptide according to claim 80, wherein the percentage identity to any one of SEQ ID Nos: 2, 6, 8, 10, 12 or 14 is at least 60%.

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- 82. The recombinant cellulose biosynthetic polypeptide according to claim 81, wherein the percentage identity to any one of SEQ ID Nos: 2, 6, 8, 10, 12 or 14 is at least 80%.
- 83. The recombinant cellulose biosynthetic polypeptide according to claim 82, comprising a sequence of amino acids substantially as set forth in any one of SEQ ID Nos: 2, 6, 8, 10,

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12 or 14.

- 84. A method of altering the mechanical properties of a cell wall, said method comprising expressing the isolated nucleic acid molecule according to any one of claims 1 to 29 in the
 5 antisense orientation in said cell for a time and under conditions sufficient for the level of non-crystalline β-1,4-glucan to increase in said cell.
 - 85. The method according to claim 84 wherein the non-crystalline β -1,4-glucan is cross-linked to cellulose microfibrils.

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- 86. The method according to claim 84 or 85 wherein the cell wall normally has a high ratio of cellulose to hemicelluloses.
- 87. The method according to any one of claims 84 to 86, wherein the nucleic acid15 molecule expressed in the antisense orientation is contained within an antisense molecule or ribozyme molecule.
 - 88. The method according to any one of claims 84 to 87, wherein the cell wall is a plant cell wall.

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89. The method according to claim 88, wherein the plant is selected from the list comprising Arabidopsis thaliana, Gossypium hirsutum (cotton), Oryza sativa (rice), Eucalyptus ssp., Brassica ssp., wheat, barley, maize, hemp, jute, flax, and woody plants such as Pinus ssp., Populus ssp., Picea spp., amongst others.

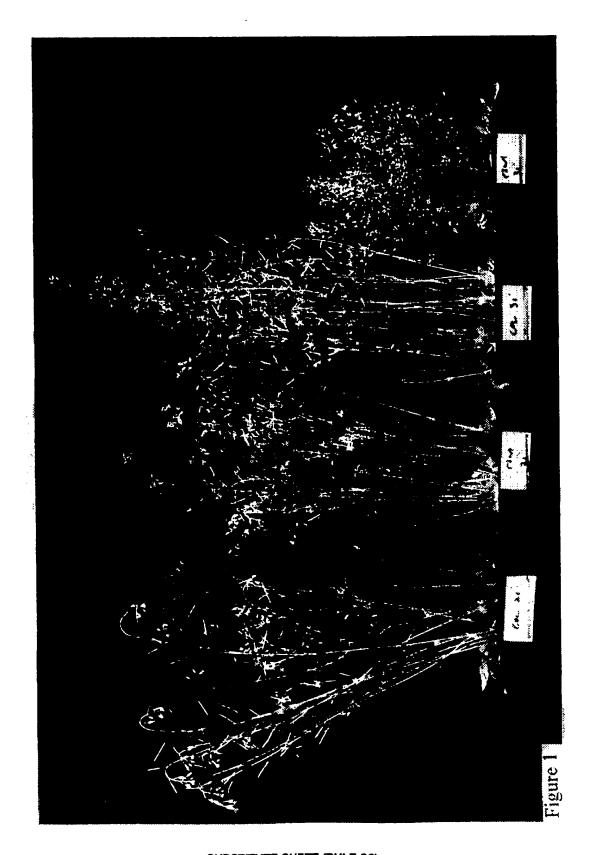
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- 90. An antibody molecule which binds to the recombinant polypeptide according to any one of claims 78 to 83 or a homologue, analogue or derivative thereof.
- 91. A transgenic plant transformed with the isolated nucleic acid molecule according to 30 any one of claims 1 to 29 or a genetic construct according to any one of claims 30 to 36.

92. The transgenic plant according to claim 91, wherein said plant is selected from the list comprising Arabidopsis thaliana. Gossypium hirsutum (cotton), Oryza sativa (rice), Eucalyptus ssp., Brassica ssp., wheat, barley, maize, hemp, jute, flax, and woody plants such as Pinus ssp., Populus ssp., Picea spp., amongst others.

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- 93. Use of an isolated nucleic acid molecule according to any one of claims 1 to 29 to modify the cellulose content of a cell.
- 94. Use according to claim 93, wherein if the nucleic acid molecule according to any one 10 of claims 1 to 29 is expressed in the sense orientation in said cell, the level of cellulose therein is increased.
- 95. Use according to claim 93, wherein if the nucleic acid molecule according to any one of claims 1 to 29 is expressed in the antisense orientation in said cell, the level of cellulose15 therein is decreased.
 - 96. Use according to claim 95, wherein said cell is further characterised by increased non-crystalline β -1,4-glucan content and/or starch content.
- 20 97. Use according to claim 95 or 96, wherein said cell is further characterised by increased cross-linking of non-crystalline β-1,4-glucan to cellulose.
 - 98. Use according to any one of claims 93 to 97, wherein the cell is a plant cell.
- 25 99. Use according to claim 98 wherein the plant is selected from the list comprising Arabidopsis thaliana, Gossypium hirsutum (cotton), Oryza sativa (rice), Eucalyptus ssp., Brassica ssp., wheat, barley, maize, hemp, jute, flax, and woody plants such as Pinus ssp., Populus ssp., Picea spp., amongst others.



SUBSTITUTE SHEET (RULE 26)



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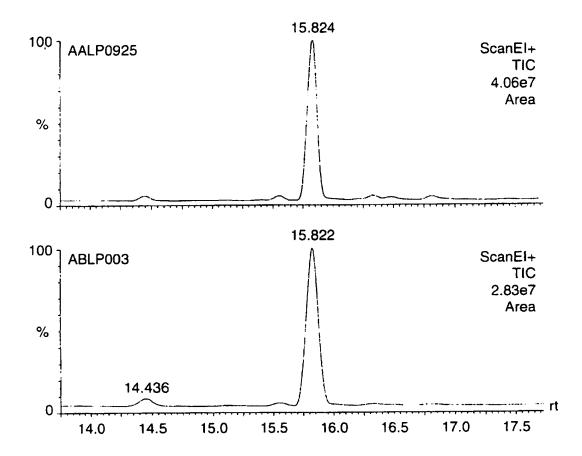


Figure 3

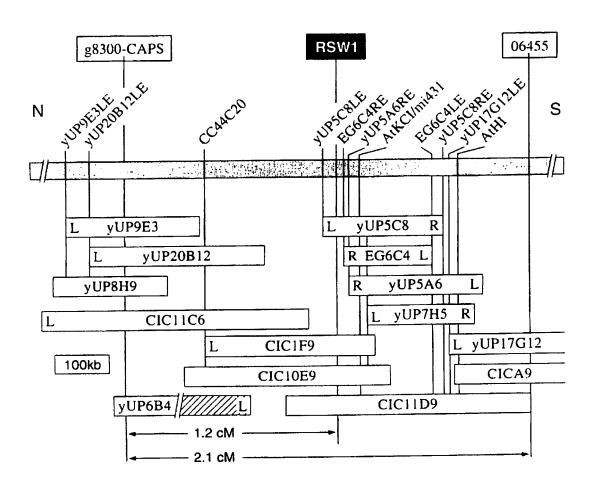


Figure 4

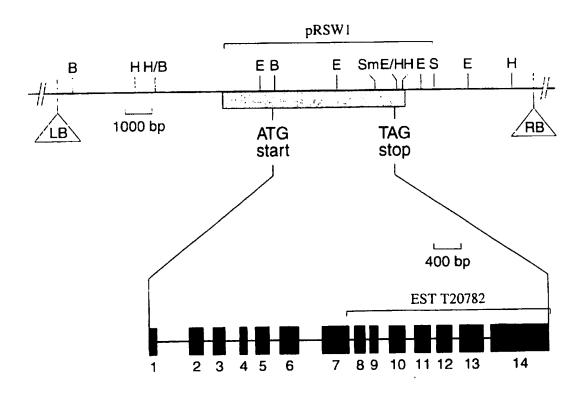
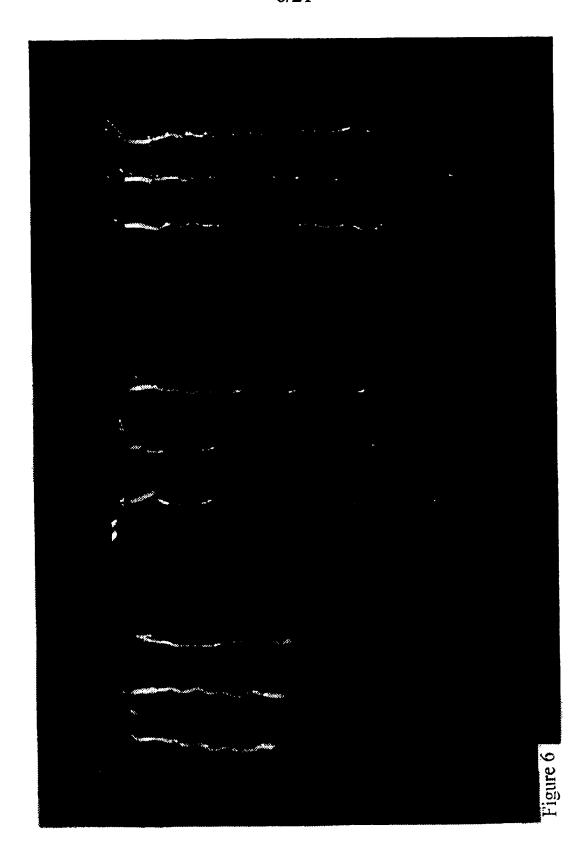
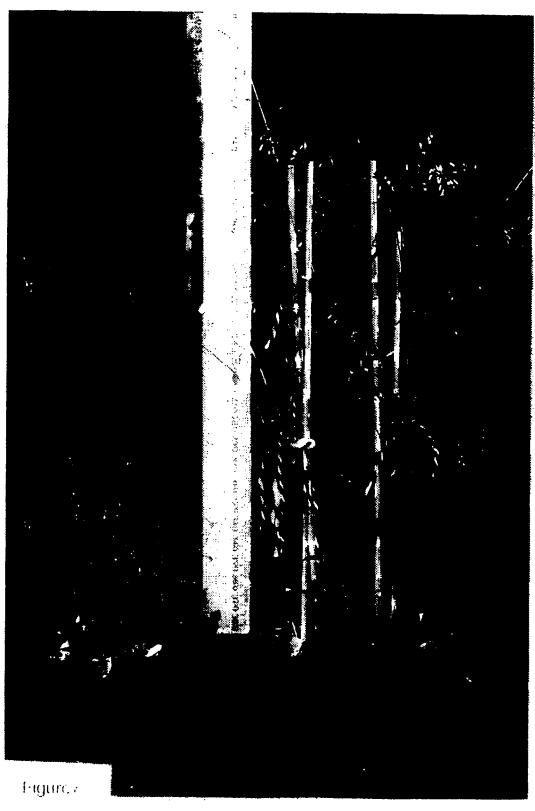


Figure 5



SUBSTITUTE SHEET (RULE 26)



SUBSTITUTE SHEET (RULE 26)

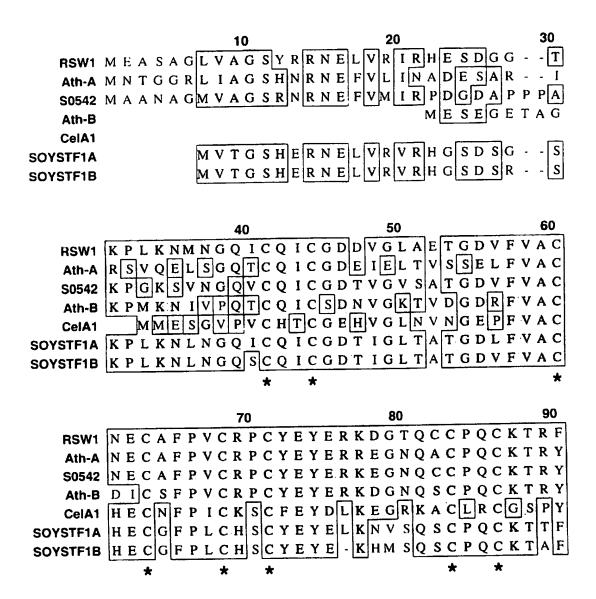


Figure 8

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Cont I Cont II Cont II Cont IV Cont V Cont VI Cont VII Cont VIII Cont IX Cont X

09 120 **NECAFPVCRPCYEYERKEGNQCCPQCKTRYKRHKGCPRVQGDEEEEDVDDLDNEFHYKHG** DICSFPVCRPCYEYERKDGNQSCPQCKTRYKRLKGSPAIPGDKDEDGLADEGTVEFNYPQ MEASAGLVAGSYRRNELVRIRHESDGG..TKPLKNMNGQICQICGDDVGLAETGDVFVAC MNTGGRLIAGSHNRNEFVLINADESAR..IRSVQELSGQTCQICGDEIELTVSSELFVAC **MAANAGMVAGSRNRNEFVMIRPDGDAPPPAKPGKSVNGQVCQICGDTVGVSATGDVFVAC** MESEGETAGKPMKNIVPQTCQICSDNVGKTVDGDRFVAC MMESGVPVCHTCGEHVGLNVNGEPFVAC **NECAFPVCRPCYEYERKDGTQCCPQCKTRFRRHRGSPRVEGDEDDDVDD1ENEFNYAQG NECAFPVCRPCYEYERREGNQACPQCKTRYKRIKGSPRVDGDDEEEEDIDDLEYEFDHGM** HECNFPICKSCFEYDLKEGRKACLRCGSPYDENLLDDVEKATGDQSTMAAHLNKSQDVGI 50 100 90 80 **D48636** 048636 CelA1 Ath-A Ath-B Ath-A **S0542** Ath-B CelA2 S0542 CelA2 CelA1 RSW1 RSW1

FIGURE 9 (CONT I)

| | 130 | 140 | 150 | 160 | 170 | 180 |
|--------|---|--|--------------------|-------------------|--|-----|
| RSW1 | ANKA | RHQRHGEEFSSSSRHESQPIPLLTHGHTVSGEIRTPDTQSVRTT | SSSRHESQPI | PLLTHGHTVS | GEIRTPDTQSV | RTT |
| Ath-A | DPEHAAEAALSSRLNTGRGGLDSAPPGSQIPLLTYCDEDADMYSDRHALIVPPSTGYGNR | TGRGGLDSAPP | GSQIPLLTYC | DEDADMYSDR | HALIVPPSTGY | GNR |
| S0542 | NGKGPEWQI | QRQGEDVDLSSSSRHEQHRIPRLTSGQQISGEIPDASPDRHSIR | SSSRHEQHRI | PRLTSGQQIS | GEIPDASPDRH | SIR |
| Ath-B | K. EKISERMLGWHLTRGKGEEMGEPQYDKEVSHNHLPRLTSRQDTSGEFSAASPERLSVS | RGKGEEMGEPQ | YDKEVSHNHI | PRLTSRODTS | GEFSAASPERI | SVS |
| Cel-A1 | | | • | | • | |
| Cel-A2 | | | | | | |
| D48636 | | | | | | |
| | 190 | 200 | 210 | 220 | 230 | 240 |
| RSW1 | SGPLGPSDRNAISSPYIDPRQPVPVRIVDPSKDLNSYGLGNVDWKERVEGWKLKQEKNML | YIDPRQPVPVR | LIVDPSKDLNS | YGLGNVDWKE | RVEGWKLKQEK | NML |
| Ath-A | VYPAF | . PAPFTDSSAPPQARSMVPQKDIAEYGYGSVAWKDRMEVWKRRQGEKLQ | SMVPQKDIAE | YGYGSVAWKD | RMEVWKRRQGE | KLQ |
| S0542 | | .TSSYVDPSVPVPVRIVDPSKDLNSYGINSVDWQERVASWRNKQDKNMM | LIVDPSKDLNS | KGINSNDMÕE | RVASWRNKQDK | NMM |
| Ath-B | | . IAGGKRLPYSSDVNQSPNRRIVDPVGLGNVAWKERVDGWKMKQEKNTG | IQSPNRRIVDE | VGLGNVAWKE | RVDGWKMKQEK | NTG |
| Cel-A1 | | HARHIS | SVSTLDSEM | EDNGNS I WKN | HARHISSVSTLDSEMAEDNGNSIWKNRVESWKEKKNKKKK | KKK |
| Cel-A2 | | | | | | |
| D48636 | | | ST | TRPGNVAWKE | STTRPGNVAWKERVDGWKLKQDKGAI | GAI |
| FIGURE | FIGURE 9 (CONT II) | | | | | |

| | | 250 | 260 | 270 | 280 | 290 | 300 |
|--------|---------------|-----------|--------------------|--------------------|-------------------|---|-------------|
| RSW1 | QMT | GKYHEG | KGGEIEGTGS | SNGEELQMADI | TRLPMSRVV | QMTGKYHEGKGGEIEGTGSNGEELQMADDTRLPMSRVVPIPSSRLTPYRVVIIL | 'IIL |
| Ath-A | VIK | HEGGNIN | GRGSNDDDDEI | CDDPDMPMMDI | GROPLSRKL | VIKHEGGNNGRGSNDDDELDDPDMPMMDEGRQPLSRKLPIRSSRINPYRMLILC | IIC |
| S0542 | QVA | NKYPEA | RGGDMEGTGS | SNGEDIQMVDI | MARLPLSRIV | QVANKYPEARGGDMEGTGSNGEDIQMVDDARLPLSRIVPIPSNQLNLYRIVIIL | 'IIL |
| Ath-B | PV | STQAASERG | GVDIDASTD | [LADEALLND] | SARQLLSRKV | PVSTQAASERGGVDIDASTDILADEALLNDEARQLLSRKVSIPSSRINPYRMVIML | 'IML |
| Cel-Al | PAT | TK | VEREAEIPPI | SQQMEDKPAPI | ASQPLSTIL | . TKVEREAEIPPEQQMEDKPAPDASQPLSTIIPIPKSRLAPYRTVIIM | /IIM |
| Cel-A2 | | | | | | | |
| D48636 | PMTNGT | SIAPSEGRG | VGDIDASTD | NMEDALLND | TROPLSRKV | PMTNGTSIAPSEGRGVGDIDASTDYNMEDALLNDETRQPLSRKVPLPSSRINPYRMVIVL | 'IVL |
| | | | | | | | |
| | | 310 | 320 | 330 | 340 | 350 | 360 |
| RSW1 | RLIILC | FFLQYRTTH | PVKNAYPLWI | TRAICEIME | AFSWLLDQFP | RLIILCFFLQYRTTHPVKNAYPLWLTSVICEIWFAFSWLLDQFPKWYPINRETYLDRLAI | LAI |
| Ath-A | RLAILG | LFFHYRILH | PVNDAYGLWI | TRAICEIME | AVSWILDQFP | RLAILGLFFHYRILHPVNDAYGLWLTSVICEIWFAVSWILDQFPKWYPIERETYLDRLSL | TST |
| S0542 | RLIILM | FFFQYRVTH | PVRDAYGLW] | CASVICEIWE | PLSWLLDQFP | RLIILMFFFQYRVTHPVRDAYGLWLVSVICEIWLPLSWLLDQFPKWYPINRETYLDRLAL | SI_AI |
| Ath-B | RLVILC | LFLHYRITN | PVPNAFALW | CVSVICEIWE | ALSWILDQFP | RLVILCLFLHYRITNPVPNAFALWLVSVICEIWFALSWILDQFPKWFPVNRETYLDRLAL | YLAL |
| Cel-A1 | RLIILG | LFFHYRVTN | PVDSAFGLW | LTSVICEIWE | AFSWVLDQFP | RLIILGLFFHYRVTNPVDSAFGLWLTSVICEIWFAFSWVLDQFPKWYPVNRETYIDRLSA | LSA |
| Cel-A2 | | | | | | | |
| D48636 | RLVVLS | IFLHYRITN | PVRNAYPLW | LLSVICEIWE | ALSWILDQFP | RLVVLSIFLHYRITNPVRNAYPLWLLSVICEIWFALSWILDQFPKWFPINRETYLDRLAL | SLAL |

FIGURE

| | 370 380 390 400 410 420 | _ |
|--------|--|-----|
| RSWI | RYDRDGEPSOLVPVDVFVSTVDPLKEPPLVTANTVLSILSVDYPVDKVACYVSDDGSAML | _ |
| Ath-A | RYEKEGKPSGLAPVDVFVSTVDPLKEPPLITANTVLSILAVDYPVDKVACYVSDDGAAML | _ |
| S0542 | RYDREGEPSQLAPIDVFVSTVDPLKEPPLITANTVLSILAVDYPVDKVSCYVSDDGSAML | _ |
| Ath-B | RLVILCLFLHYRITNPVPNAFALWLVSVICEIWFALSWILDQFPKWFPVNRETYLDRLAL | _ |
| Cel-A1 | RYEREGEPDELAAVDFFVSTVDPLKEPPLITANTVLSILALDYPVDKVSCYISDDGAAML | _ |
| Cel-A2 | | |
| D48636 | RYDREGEPSQLAAVDIFVSTVDPMKEPPLVTANTVLSILAVDYPVDKVSCYVSDDGAAML | _ |
| | 430 440 450 480 | |
| r we w | FAKKWVPFCKKFNIEPRAPEFYFAQKIDYLKDKIQPS | 5.3 |
| Ath-A | TFEALSDTAEFARKWVPFCKKFNIEPRAPEWYFSQKMDYLKNKVHPAFVRERRAMKRDYE | c-3 |
| S0542 | TFEALSETAEFARKWVPFCKKHNIEPRAPEFYFAQKIDYLKDKIQPSFVKERRAMKREYE | 5-7 |
| Ath-B | SFESLAETSEFARKWVPFCKKYSIEPRAPEWYFAAKIDYLKDKVQTSFVKDRRAMKREYE | r_7 |
| Ce1-A1 | TFESLVETADFARKWVPFCKKFSIEPRAPEFYFSQKIDYLKDKVQPSFVKERRAMKRDYE | F-3 |
| Ce1-A2 | RRWVPFCKKHNVEPRAPEFYFNEKIDYLKDKVHPSFVKERRAMKREYE | r-3 |
| D48636 | TFDALAETSEFARKWVPFVKKYNIEPRAPEWYFSQKIDYLKDKVHPSFVKDRRAMKREYE | f-7 |

FIGURE 9 (CONT IV)

| | 490 | 200 | 510 | 520 | 530 | 540 |
|--------|---|---------------------|------------|-------------------|---|-------|
| RSW1 | EFKVRINALVAKAQKI PEEGWTMQDGT PWPGNNTRDHPGMIQVFLGHSGGLDTDGNEL PR | KIPEEGWTMQD | GTPWPGNNTR | DHPGMIQVFL | GHSGGLDTDGNE | .PR |
| Ath-A | EFKVKINALVATAQ | KVPEEGWTMQD | GTPWPGNNVR | DHPGMIQVFL | ATAQKVPEEGWTMQDGTPWPGNNVRDHPGMIQVFLGHSGVRDTDGNELPR | .PR |
| S0542 | EFKVRINALVAKAQKVPEEGWTMADGTAWPGNNFRDHPGMIQVFLGHSGGLDTDGNELPR | KVPEEGWTMAD | GTAWPGNNFR | DHPGMIQVFL | GHSGGLDTDGNE | .PR |
| Ath-B | EFKIRINALVSKAL | KCPEEGWVMQD | GTPWPGNNTG | DHPGMIQVFL | SKALKCPEEGWVMQDGTPWPGNNTGDHPGMIQVFLGQNGGLDAEGNELPR | LPR |
| Cel-A1 | EYKIRINALVAKAQ | KTPDEGWTMQD | GTSWPGNNPR | DHPGMIQVFL | AKAQKTPDEGWTMQDGTSWPGNNPRDHPGMIQVFLGYSGARDIEGNELPR | JPR |
| Ce1-A2 | EFKVRINALVAKAQKKPEEGWVMQDGTPWPGNNTRDHPGMIQVYLGSAGALDVDGKELPR | KKPEEGWVMQD | GTPWPGNNTR | DHPGMIQVYL | GSAGALDVDGKE | J.P.R |
| D48636 | EFKVRINGLVAKAQKVPEEGWIMQDGTPWPGNNTRDHPGMIQVFLGHSGGLDTEGNELPR | KVPEEGWIMQD | GTPWPGNNTR | DHPGMIQVFL | GHSGGLDTEGNE | JPR |
| | | | | | | |
| | 550 | 560 | 570 | 580 | 590 | 009 |
| RSW1 | LIYVSREKRPGFQHHKKAGAMNALIRVSAVLTNGAYLLNVDCDHYFNNSKAIKEAMCFMM | HKKAGAMNALI | RVSAVLTNGA | XLLNVDCDHY | FINNSKAIKEAMCI | FMM |
| Ath-A | LVYVSREKRPGFDHHKKAGAMNSLIRVSAVLSNAPYLLNVDCDHYINNSKAIRESMCFMM | HKKAGAMNSL1 | RVSAVLSNAP | YLLNVDCDHY | INNSKAIRESMC | MMF |
| S0542 | LVYVSREKRPGFQHHKKAGAMNALIRVSAV | HKKAGAMNAL I | RVSAV | | | |
| Ath-B | LVYVSREKRPGFQH | HKKAGAMNALV | RVSAVLTNGP | FILINLDCDHY | GFQHHKKAGAMNALVRVSAVLTNGPFILNLDCDHYINNSKALREAMCFLM | FLM |
| Cel-A1 | LVYVSREKRPGYQHHKKAGAENALVRVSAVLTNAPFILNLDCDHYVNNSKAVREAMCFLM | HKKAGAENALV | RVSAVLTNAP | FILNLDCDHY | VNNSKAVREAMC | FLM |

FIGURE 9 (CONT V)

Cel-A2 D48636

LVYVSREKRPGYQHHKKAGAENALVRVSAVLTNAPFILNLDCDHYINNSKAMREAMCFLM LVYVSREKRPGFQHHKKAGAMNALVRVSAVLTNGQYMLNLDCDHYINNSKALREAMCFLM

| | 610 | 620 | 630 | 640 | 650 | 099 |
|--------|--|--------------------|----------|-------------|----------------------|-----|
| RSW1 | DPAIGKKCCYVQFPQRFDGIDLHDRYANRNIVFFDINMKGLDGIQGPVYVGTGCCFNRQA | RFDGIDLHDRY | ANRNIVFF | DINMKGLDGIC | GPVYVGTGCCFN | RQA |
| Ath-A | DPQSGKKVCYVQFPQRFDGIDRHDRYSNRNVVFFDINMKGLDGIQGPIYVGTGCVFRKQA | RFDGIDRHDRY | SNRNVVFF | DINMKGLDGIC | 2GPIYVGTGCVFR | KQA |
| S0542 | | | | | | |
| Ath-B | DPNLGKQVCYVQFPQRFDGIDKNDRYANRNTVFFDINLRGLDGIQGPVYVGTGCVFNRTA | RFDGIDKNDRY | ANRNTVFF | DINLRGLDGIC |)GPVYVGTGCVFN | RTA |
| Cel-A1 | DPQVGRDVCYVQFPQRFDGIDRSDRYANRNTVFFDVNMKGLDGIQGPVYVGTGCVFNRQA | RFDGIDRSDRY | ANRNTVFF | DVNMKGLDGIQ | QGPVYVGTGCVFN | RQA |
| Ce1-A2 | DPQFGKKLCYVQFPQRFDGIDRHDRYANRNVVFFDINMLGLDGLQGPVYVGTGCVFNRQA | RFDGIDRHDRY | ANRNVVFF | DINMIGIDGEC | JGPVYVGTGCVFN | RQA |
| D48636 | DPNLGRSVCYVQFPQRFDGIDRNDRYANRNTVFFDINLRGLDGIQGPVYVGTGCVFNRTA | RFDGIDRNDRY | ANRNTVFF | DINLRGLDGIC | JGPVYVGTGCVFN | RTA |
| | 670 | 089 | 069 | 700 | 710 | 720 |
| RSW1 | LYGYDPVLTEEDLEPNIIVKSCCGSRKKGKSSKKYNYE. | NIIVKSCCGSR | KKGKSSKK | YNYE | • | KRR |
| Ath-A | LYGFDAPKKKKPPGKTCNCWPKWCCLCCGLRKKSKTKA. | ICNCWPKWCCL | CCGLRKKS | KTKA | KDKKT | KKT |
| S0542 | | | | | | |
| Ath-B | LYGYEPPIKVKHKKPSLLSKLCGGSRKKNSKAKKESDK. | SLLSKLCGGSR | KKNSKAKK | ESDK | KKSGR | SGR |
| Cel-A1 | LYGYGPPSMPSFPKSSSSSCSCCCPGKKEPKDPS | ssss | CCPGKKEP | KDPS | ELYRDA | RDA |
| Cel-A2 | LYGYDPPVSEKRPKMTCDCWPSWCCCCCGGSRKKSKKKGEKKGLLGGLLYGKKKKMMGKN | ICDCWPSWCCC | CCGGSRKK | SKKKGEKKGLI | GGLLYGKKKKMM | GKN |
| D48636 | LYGYEPPIKQKKKGSFLSSLCGGRKKASKSKKKSSDK | FLSSLCGGRKK | ASKSKKKS | SDK | KKSNK | SNK |
| | | | | | | |

| | 730 | 740 | 750 | 160 | 770 | 780 |
|--------|---|--------------|-------------------|-------------------|-------------------------|-----|
| RSW1 | GINRSDSNAPLFNMEDIDEGFEGYDDERSILMSQRSVEKRFGQSPVFIAATFMEQGGIPP | DIDEGFEGYDD | ERSILMSQRS | /EKRFGQSPVI | FIAATFMEQGG | IPP |
| Ath-A | NTKETSKQIHALENVDEGVIVPVSNVEKRSEATQLKLEKKFGQSPVFVASAVLQNGGVPR | DEGVIVPVSNV | EKRSEATQLKI | JEKKFGQSPVE | ⁷ VASAVLQNGG | /PR |
| 71000 | | | | | | |
| Ath-B | HTDS.TVPVFNLDDIEEGVEGAGFDDEKALLMSQMSLEKRFGQSAVFVASTLMENGGVPP | EEGVEGAGFDD | EKALLMSQMSI | LEKRFGQSAVI | VASTLMENGG | /PP |
| Cel-Al | KREELDAAIFNLREIDNYDEYERSMLISQTSFEKTFGLSSVFIESTLMENGGVAE | DNYDEY | ERSMLISQTS | FEKTFGLSSVE | TESTLMENGG | JAE |
| Cel-A2 | YVKKGSAPVFDLEEIEEGLEG. YEELEKSTLMSQKNFEKRFGQSPVFIASTLMENGGLPE | EEGLEG. YEEL | EKSTLMSQKNI | FEKRFGQSPVF | FIASTLMENGG |]PE |
| D48636 | HVDS.AVPVFNLEDIEEGVEGAGFDDEKSLLMSQMSLEKRFGQSAAFVASTLMEYGGVPQ | EEGVEGAGFDD | EKSLLMSQMSI | LEKRFGQSAAF | *VASTLMEYGG | VPQ |
| | 790 | 800 | 810 | 820 | 0830 | 840 |
| RSW1 | TTNPATLLKEAIHVISCGYEDKTEWGKEIGWIYGSVTEDILTGFKMHARGWISIYCNPPR | SCGYEDKTEWG | KEIGWIYGSVJ | FEDILTGFKM | HARGWISIYCN | PPR |
| Ath-A | NASPACLLREAIQVISCGYEDKTEWGKEIGWIYGSVTEDILTGFKMHCHGWRSVYCMPKR | SCGYEDKTEWG | KEIGWIYGSV | FEDILTGFKM | ICHGWRSVYCM | PKR |
| S0542 | | | | | | |
| Ath-B | SATPENFLKEAIHVISCGYEDKSDWGMEIGWIYGSVTEDILTGFKMHARGWRSIYCMPKL | SCGYEDKSDWG | MEIGWIYGSVT | FEDILTGFKM | HARGWRSIYCM | PKL |
| Cel-Al | SANPSTLIKEAIHVISCGYEEKTAWGKEIGWIYGSVTEDILTGFKMHCRGWRSIYCMPLR | SCGYEEKTAWG | KEIGWIYGSV | FEDILTGFKM | HCRGWRSIYCM | PLR |
| Cel-A2 | GINSTSLIKEAIHVISCGYEEKTEWGKEIGWIYGSVTEDILTGFKMHCRGWKSVYCVPKR | SCGYEEKTEWG | KEIGWIYGSV | FEDILTGFKM | ICRGWKSVYCV | PKR |
| D48636 | SATPESLLKEAIHVISCGYEDKTEWGTEIGWIYGSVTEDILTGFKMHARGWRSIYCMPKR | SCGYEDKTEWG | TEIGWIYGSV. | FEDILTGFKM | HARGWRSIYCM | PKR |

| | 850 | 860 | 870 | 880 | 96 068 | 900 |
|--------|--|-------------|------------|--------------------|---|-----|
| RSW1 | PAFKGSAPINLSDRLNQVLRWALGSIEILLSRHCPIWYGYHG.RLRLLERIAYINTIVYP | NOVLRWALGSI | EILLSRHCPI | WYGYHG.RLI | RLLERIAYINTIVY | ΥP |
| Ath-A | AAFKGSAPINLSDRL | HQVLRWALGSV | EIFLSRHCPI | WYGYGG.GL | NLSDRLHQVLRWALGSVEIFLSRHCPIWYGYGG.GLKWLERFSYINSVVYP | ΚÞ |
| S0542 | 1 | | | | | 9 |
| Ath-B | PAFKGSAPINLSDRLNQVLRWALGSVEILFSRHCPIWYGYNG.RLKFLERFAYVNTTIYP | NOVLRWALGSV | EILFSRHCPI | WYGYNG.RLI | KFLERFAYVNTTI Y | ΚÞ |
| Cel-A1 | PAFKGSAPINLSDRLHQVLRWALGSVEIFLSRHCPLWYGFGGGRLKWLQRLAYINTIVYP | HQVLRWALGSV | EIFLSRHCPL | WYGFGGGRLI | KWLQRLAYINTIVY | ΥЪ |
| Cel-A2 | PAFKGSAPINLSDRL | HQVLRWALGSV | EIFLSRHCPL | WYGYGG.KLI | NLSDRLHQVLRWALGSVEIFLSRHCPLWYGYGG.KLKWLERLAYINTIVYP | ΚЪ |
| D48636 | PAFKGSAPINLSDRL | NQVLRWALGSV | EILFSRHCPI | WYGYGG.RLI | NLSDRLNQVLRWALGSVEILFSRHCPIWYGYGG.RLKFLERFAYINTTIYP | ΧÞ |
| | 910 | 920 | 930 | 940 | 920 96 | 960 |
| RSW1 | ITSIPLIAYCILPAFCLITDRFIIPEISNYASIWFILLFISIAVTGILELRWSGVSIEDW | CLITDRFIIPE | ISNYASIWFI | LLFISIAVT (| GILELRWSGVSIE L | ΜO |
| Ath-A | WTSLPLIVYCSLPAVCLLTGKFIVPEISNYAGILFMLMFISIAVTGILEMQWGGVGIDDW | CLLTGKFIVPE | ISNYAGILFM | LMFISIAVT | SILEMQWGGVGIDE | MO |
| S0542 | | | | | | |
| Ath-B | ITSIPLLMYCTLLAVCLFTNQF1IPQISNIASIWFLSLFLSIFATGILEMRWSGVGIDEW | CLFTNQFIIPQ | ISNIASIWFL | SLFLSIFAT | GILEMRWSGVGIDE | EΣ |
| Cel-A1 | FTSLPLIAYCSLPAICLLTGKF1IPTLSNLASVLFLGLFLSIIVTAVLELRWSGVSIEDL | CLLTGKFIIPT | LSNLASVLFL | GLFLSIIVT | AVLELRWSGVSIEL | DI |
| Cel-A2 | FTSIPLLAYCTIPAVCLLTGKFIIPTLSNLTSVWFLALFLSIIATGVLELRWSGVSIQDW | CLLTGKFIIPT | LSNLTSVWFL | ALFLSIIAT | GVLELRWSGVSIQE | MO |
| D48636 | LTSIPLLIYCVLPAICLLTGKFIIPEISNFASIWFISLFISIFATGILEMRWSGVGIDEW | CLLTGKFIIPE | ISNFASIWFI | SLFISIFAT | GILEMRWSGVGIDE | ΕW |

FIGURE 9 (CONT VIII)

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1080 PPTTVLLVNLIGIVAGVSYAVNSGYQSWGPLFGKLFFALWVIAHLYPFLKGLLGRQNRTP PPTTLLIINIIGVIVGVSDAISNGYDSWGPLFGRLFFALWVIVHLYPFLKGMLGKQDKMP PPTTLLIVNLVGVVAGVSYAINSGYQSWGPLFGKLFFAFWVIVHLYPFLKGLMGRQNRTP PPTTLLIVNMVGVVAGFSDALNKGYEAWGPLFGKVFFSFWVILHLYPFLKGLMGRONRTP PPTTLIILNMVGVVAGVSDAINNGYGSWGPLFGKLFFAFWVILHLYPFLKGLMGRONRTP PPTTILIINLVGVVAGISYAINSGYQSWGPLFGKLFFAFWVIVHLYPFLKGLMGRQNRTP WRNEQFWVIGGVSAHLFAVFQGLLKVLAGVDTNFTVTAKAAD.DTEFGELYLFKWTTLLI WRNEQFWVIGGISAHLFAVFQGLLKVLAGIDTNFTVTSKASDEDGDFAELYMFKWTTLLI WRNEQFWVIGGTSAHLFAVFQGLLKVLAGIDTNFTVTSKATDEDGDFAELYIFKWTALLI WRNEQFWVIGGASSHLFALFQGLLKVLAGVNTNFTVTSKAAD.DGAFSELYIFKWTTLLI WRNEQFWVIGGVSAHLFAVFQGILKVLAGIDTNFTVTSKASDEDGDFAELYLFKWTTLLI WRNEOFWVIGGVSAHLFAVFQGFLKMLAGIDTNFTVTAKAAD.DADFGELYIVKWTTLLI 1070 1010 1000 1060 1050 990 980 1040 1030 970 Cel-A2 **D48636** Cel-A2 **D48636** Cel-A1 Cel-A1 Ath-B Ath-B Ath-A Ath-A **S0542** S0542 RSW1 RSW1

FIGURE 9 (CONT IX)

TIVIVWSVLLASIFSLLWVRINPFVDANPNANNFNGKGGVF 1100 1090

Ath-A RSW1

TIIVVWSILLASILTLLWVRINPFVAK.GGPVLEICGLNCGN

S0542

TIVVLWSVLLASVFSLVWVRINPFVSTADSTTVSQSCISIDC TIVVVWSVLLASIFSLLWVRIDPFTSRVTGPDILECGINC TIVVLWSILLASIFSLVWVRIDPFLPKQTGPVLKQCGVEC Cel-A1 Ath-B

TIVVVWAILLASIFSLLWVRIDPFTTRVTGPDTQTCGINC Cel-A2 D48636

6 (CONT X) FIGURE

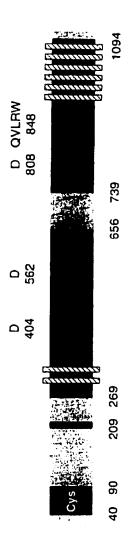
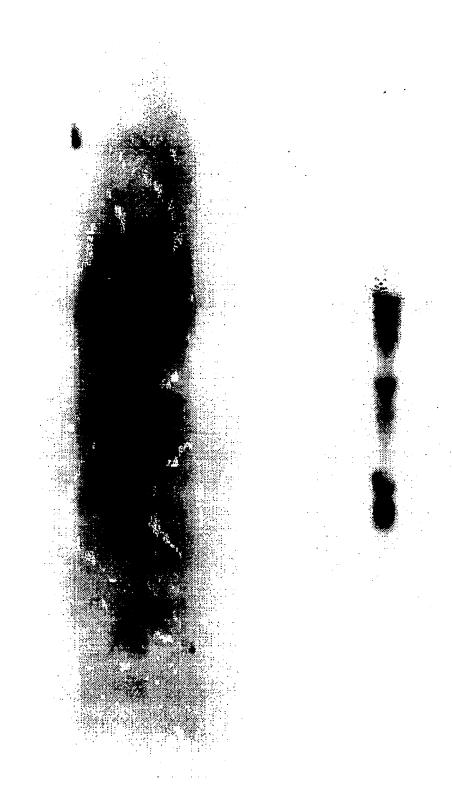


FIGURE 10



INTERNATIONAL SEARCH REPORT

CLASSIFICATION OF SUBJECT MATTER

A.

International Application No. PCT/AU 97/00402

| According to | International Patent Classification (IPC) or to both national classification and IPC | | |
|---|--|---|--|
| В. | FIELDS SEARCHED | | |
| | umentation scarched (classification system followed by classification symbols) ic Database Box below | | |
| Documentation See Electron | searched other than minimum documentation to the extent that such documents are included in ic Database Box below | the fields searched | |
| WPAT. Med | base consulted during the international search (name of data base and, where practicable, search alline, ChemAbs, Genebank, Swiss Prot, EMBL as: Cellulose Biosynthesis, Cellulose Synthase, Sequence ID# 2. | terms used) | |
| С. | DOCUMENTS CONSIDERED TO BE RELEVANT | | |
| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. | |
| x x | WO 91/13988 (THE BOARD OF REGENTS, THE UNIVERSITY OF TEXAS SYSTEM), 19 September 1991 see whole document WO 92/18631 (WEYERHAESUR COMPANY) 29 October 1992 see whole document | 1-4, 14-16, 30-32 1-4, 14-16 | |
| Х | WO 90/12098 (CETUS CORPORATION) 18 October 1990 see whole document | 1-4, 14-16 | |
| | Further documents are listed in the continuation of Box C See patent family annex | | |
| "A" docum not con "E" earlier interna "L" docum or whi anothe "O" docum exhibit "P" docum | later document published after the in priority date and not in conflict with understand the principle or theory understan | the application but cited to derlying the invention claimed invention cannot sidered to involve an taken alone claimed invention cannot step when the document in the documents, such on skilled in the art | |
| Date of the actu 14 August 1997 | Date of mailing of the international search 1 8 AUG 1997 | ch report | |
| | ing address of the ISA/AU INDUSTRIAL PROPERTY ORGANISATION 2606 Facsimile No.: (06) 285 3929 Authorized officer Philippa Wyrdeman JIM CHAN Telephone No.: (06) 283 2340 | | |

INTERNATIONAL SEARCH REPORT

... ternational Application No.

PCT/AU 97/00402

| Box 1 | Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet) | |
|----------|---|--|
| This Int | ernational Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following | |
| 1. | Claims Nos.: | |
| | because they relate to subject matter not required to be searched by this Authority, namely: | |
| 2. | Claims Nos.: because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically: | |
| , | China Nac | |
| 3. | Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a) | |
| Box II | Observations where unity of invention is lacking (Continuation of item 2 of first sheet) | |
| This Int | ernational Searching Authority found multiple inventions in this international application, as follows: | |
| | | |
| 1. | As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims | |
| 2. | As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee. | |
| 3. | As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.: | |
| 4. | No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: | |
| Remari | k on Protest The additional search fees were accompanied by the applicant's protest. | |
| | No protest accompanied the payment of additional search fees. | |
| | | |

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No. PCT/AU 97/00402

This Annex lists the known "A" publication level patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

| Patent Do | cument Cited in Search Report | | | Patent | Family Member | | |
|-----------|----------------------------------|----|----------|--------|---------------|----|---------|
| wo | 9113988 | AU | 75569/91 | | | | |
| wo | 9012098 | AU | 54373/90 | CA | 2014264 | EP | 471687 |
| | | IL | 94053 | NZ | 233312 | US | 5268274 |
| wo | 9218631 | US | 5268274 | NZ | 233312 | CA | 2014264 |
| | | IL | 94053 | AU | 54373/90 | EP | 471687 |

END OF ANNEX

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